Amsterdam UMC
University Medical Centers

Cancer Center Amsterdam

Site visit report

2017-2022

Colophon

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Word of introduction

The research institute Cancer Center Amsterdam as we know it today was initiated in 2016 ahead of the merger of VUmc and AMC, now Amsterdam UMC. Joining the oncological research of these two medical centers instantly led to formation of the largest concentration of cancer research in the Netherlands within one institute, matching the size and scope of international comprehensive cancer centers. It logically expressed the ambition to become a world-leading research institution with a vision to improve cancer care by connecting fundamental biological and immunological insight with clinical needs and vice versa by connecting clinical reality with science to push translation of our research. Its embedding in Amsterdam UMC provides a unique opportunity to make a change, which affirms our believe that our science of today is the therapy of tomorrow.

The research institute houses well over 1200 fundamental, translational and clinical researchers and provides a platform for excellence. Among these we host >550 PhD candidates, almost invariably appointed on external grants, for which Cancer Center Amsterdam provides a world-class educational platform. An impressive total of 506 PhDs have graduated in the last 6 years.

In the same period (2017-2022), our researchers acquired over 240 million euro in competitive funding and published a total of 6744 peer-reviewed publications. More importantly, they have made game-changing discoveries and implemented innovations that impacted clinical routine and as a consequence patient's cure and/or quality of life. We have seen implementation of neoadjuvant therapy in pancreatic, metastatic colorectal and esophageal cancer, therapies that emanate from clinical trials (co-)led by our researchers. We have seen our research on shared decision making move into practice, changes in the way hemato-oncology patients are treated and we have seen the launch of an imaging building with total body PET-CT imaging.

Despite these impressive achievements, the past years have been challenging. Merging two large medical centers and lateralization of all oncological research and care to one location has shown to be a complex process, which is still far from finished. Maintaining quality of research and care, or even better, fulfilling the ambition to improve has been highly demanding. Next to this, the past years were colored by the impact of the pandemic on society, our health care system and as a consequence our science. Right before the first lock down Cancer Center Amsterdam had its yearly retreat where over 400 of our researchers met. Normally these retreats are a breeding ground for new ideas and collaborations, but this time all of this excitement and plans had to be parked as a lot of our preclinical research came to a full stop. Clinical research was continued where possible, but novel trials were postponed and inclusion rates dropped tremendously due to a changing clinical landscape. This period required our researchers to be creative, adaptive, but above all patient and we are tremendously proud by the resilience the cancer center's researchers have shown. Intriguingly, we have seen a peak in publications and PhD graduations during the pandemic years, which we believe reflects the need to move from bench to (home)desk and prioritized writing articles and theses. Next to this positive side-effect, COVID-19 also taught us that innovative translational science requires interaction and team science. Being deprived of effortless interactions quickly revealed how dependent our current scientific efforts are on multidisciplinary teams and on the possibility to have live meetings or simple hallway chats. Cancer Center Amsterdam therefore tries to emerge from the pandemic by providing this platform of interaction and by endorsing and enticing team science.

During the last years the institute's directory also realized that to achieve a truly translational institute additional steps needed to be taken on top of the alliance of both research units. In 2020 Cancer Center Amsterdam therefore embraced another challenge building a cancer center where Science and Care are connected. Stepping forward into a more comprehensive cancer center embedded in a larger university medical center with all medical specialties represented has the potential to make a real difference. Although we still have a long way to go we are proud to say that our central motto "connecting science and care" is well under way. Thanks to the flexibility of our staff, the creative minds and the relentless strive for innovation for our patients, we are drawing closer to a full alliance of all cancer-related activities on one location. We are convinced the connection between researchers, clinicians and patients is what is needed to progress and are looking towards the outside world to join forces and to further improve care for our patients of today and tomorrow.

Jan Paul Medema
Scientific Director Cancer Center Amsterdam
Geert Kazemier
Director Cancer Center Amsterdam

Introduction

Cancer Center Amsterdam started as a research institute that is housed within Amsterdam UMC. It was founded already well before 2016 at the VUmc, but was merged with the oncological research activities at AMC. At the start in 2016, two directors, Henk Verheul and Jan Paul Medema, one from each medical center, were appointed to guide the alliance of the institute and its research efforts. A total of more than 1200 staff, including PhD candidates, became part of this research institute, which covered the complete spectrum from basic science to translational, clinical and QoL research.

Importantly, Cancer Center Amsterdam is not an institute in the strict sense of the word as we do not appoint personnel directly, nor does the institute control research budgets. Instead, it was designed as network organization connecting researchers from a multitude of departments (n=38) and 9 divisions (Figure 1).

The main goal of Cancer Center Amsterdam is therefore to facilitate oncological research and to provide a platform for our researchers. On one hand this is done by aligning Amsterdam UMC's central investments in research with the needs of the cancer center and on the other hand by direct investments into infrastructure and excellent teams from the small budget that is allocated to the institute and the funds that our associated foundation provides. In addition, Cancer Center Amsterdam aims to identify our excellent areas of research and novel developments and aids in the acquisition of funding for our research teams.

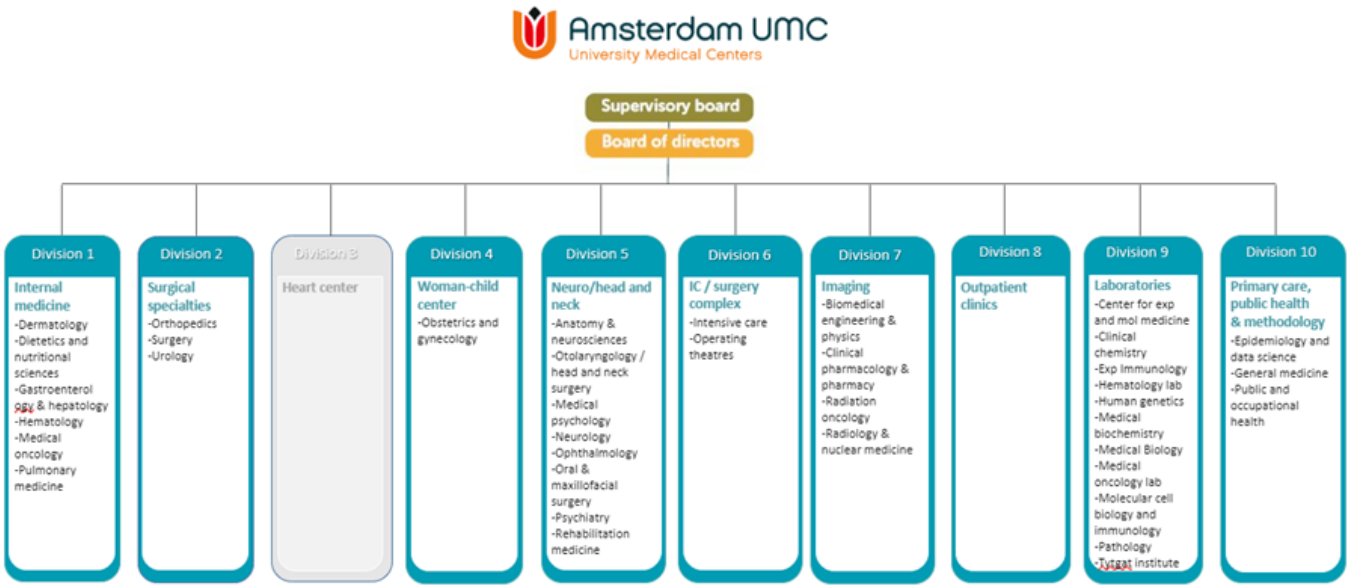


Figure 1. Listing of divisions and departments within Cancer Center Amsterdam

Embedding of Cancer Center Amsterdam

Amsterdam UMC is the largest medical center in the Netherlands with around 17000 employees that arose from the merger of AMC and VUmc in 2018. It has four main pillars of activity, being complex care, research, education and valorization, and a board of directors that consists of 5 members. Prof. Chris Polman is chair and dean of the VU faculty of Medicine, Prof. Hans van Goudoever is vice-chair and dean of the UvA faculty, Mr. Henk Snapper is the Chief Financial Officer, and the other members are Prof. Mark Kramer and Dr. Karen Kruijthof (see picture 1).

The merger resulted in the foundation of one medical center that encompasses two medical faculties (Vrije Universiteit Amsterdam and University of Amsterdam). The Amsterdam UMC professors, and as a consequence also the Cancer Center Amsterdam professors, therefore have an appointment within Amsterdam UMC, but are connected to one of the two universities.

Picture 1 Board of directors

A wide variety of research on all medical domains is conducted in Amsterdam UMC, To accommodate all research programs, 8 research institutes were formed with two scientific directors each. All directors are seated in the Amsterdam Research Board, which advises the Amsterdam UMC board of directors on infrastructure, legal issues, granting schemes, science registration, ethics, core facilities and many more research-related topics. Besides this general assembly, each research institute has its own structure and organization. Importantly, as the institutes work as network structures there is also a fair amount of scientists who find their home in two distinct institutes due to overlapping interests. As a result Cancer Center Amsterdam has close ties with the institutes Amsterdam Infection & Immunity, Amsterdam Public Health, Amsterdam Gastroenterology, Endocrinology & Metabolism and Amsterdam Neurosciences.

Structure of Cancer Center Amsterdam

Cancer Center Amsterdam's structure over the period of the site visit (2017-22) should be regarded in two phases, before and after 2020. As indicated, Henk Verheul and Jan Paul Medema initiated the institute and started with an in depth discussion with principle investigators (PIs) on the best organizational format of all affiliated researchers. The discussion between tumor type-specific organization versus topic-specific organization favored the last and hence 3 main research programs were founded; Cancer Biology & Immunology, Imaging & Biomarkers and Clinical Therapy and QoL. These three programs were further subdivided into themes (Figure 2 and appendix 1). To allow for an efficient start, all themes were spearheaded by 4 PIs, with a mixture of clinical and pre-clinical profiles, who were charged by building a community within their respective themes. In addition, the theme leaders were asked to identify strengths and weaknesses of their theme and to bring opportunities for improvements to the research board of Cancer Center Amsterdam. This first phase was used optimally to try and connect scientists from both locations (AMC and VUmc), to provide seed funding for research, to invest in facilities or projects that would serve the themes specifically and to identify and support excellence.

After 4 years three main changes set the scene for the next phase. First, one of the directors, Henk Verheul, left Amsterdam UMC for a new position. Second, the physical merger of clinical departments of AMC and VUmc provided Cancer

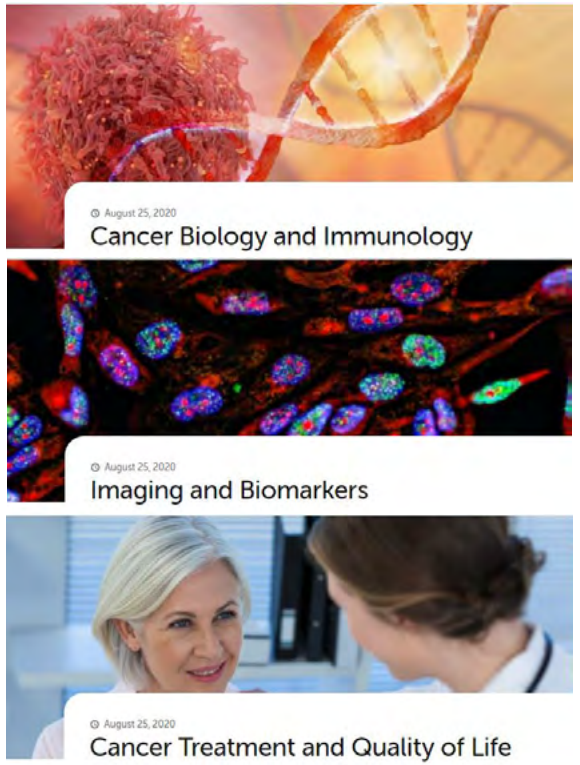


Figure 2. Research programs of Cancer Center Amsterdam

Picture 2. Daily Board Cancer Center Amsterdam

Picture 3. Support staff of the institute.

Center Amsterdam with enormous opportunities for translational and clinical research. Third, the COVID-19 pandemic and especially the success achieved in the development of therapies and vaccines, was a reiteration of an old lesson that says that intimate relations between care and research is an essential accelerator for innovation. Cancer Center Amsterdam therefore made a strategic decision to closely connect Care and Science into a more comprehensive cancer center in order to achieve our translational goals. This ambition led to the appointment of the daily board of Cancer Center Amsterdam that consists of Geert Kazemier, Sonja Zweegman, Hanneke van Laarhoven, Paul Fockens and Jan Paul Medema (Picture 2) that is supported by a team of enthusiastic and knowledgeable staff (Picture 3). Together they set the stage for an organization where all oncological care and research is represented and where strategic plans are discussed and implemented. Of note, all

members of the daily board are high profile researchers with impressive track records, but only two of them are formally responsible for the research programs of the institute, being Jan Paul Medema (scientific director) and Geert Kazemier (director). Both are seated in the research board of Cancer Center Amsterdam where they are joined by theme leaders of the respective themes.
Importantly, in this second phase of the evaluation period (2020-22) a change in the leadership of the themes was also implemented. As the first years were directed to building an alliance, having 4 theme leaders with their own network served a clear goal. In the second phase a choice was made for a more lean board and 1 theme leader was appointed per theme (Picture 4). Their role remained unchanged as they were and are still responsible for organizing their themes, identifying strength and weaknesses, feeding the research board with theme-related issues and monitoring developments in the field. On top of this the research board members have other tasks that are all aimed at aiding our strategic plans for the institute (see list of portfolios in table I).

Picture 4. Research board members

Oncology Graduate School OOA

All PhD candidates that wish to graduate at one of our partner universities are enrolled in the Doctoral School, which provides relevant information, monitors progress of our PhDs and provides general courses. Currently more than 3000 PhDs are enrolled. Importantly, the vast majority of our PhD candidates are formally employed within Amsterdam UMC and mostly hold an externally-funded position that routinely lasts 4-5 years. These positions are controlled by their respective departments and as such they are not only PhD candidates in a Doctoral School, but often also employees of Amsterdam UMC. Although the Doctoral School provides a solid general infrastructure for the PhD candidates, Cancer Center Amsterdam also has a more topical graduate school that works as an extension of the Doctoral school and is called Oncology Graduate School Amsterdam (OOA). OOA was founded well over 30 years ago as an oncological collaboration of VUmc, AMC and NKI-AvL that was aimed at training the next generation of researchers. It has evolved into a very active school that organizes topical meetings and courses, a very successful PhD retreat and oversees the development of all Amsterdam's oncological PhD candidates. (page 20 and appendix 2).

Stichting Cancer Center Amsterdam

Last but not least Cancer Center Amsterdam is blessed with a foundation called Stichting CCA. This foundation attracts funds from the private domain and has one goal which is to finance oncological research within Cancer Center Amsterdam. Two main avenues of support have been defined; the first is geared towards expensive infrastructure and equipment. The foundation is for instance the biggest private sponsor for our new research building that is currently built at location VUmc. In addition, acquisition of robotic surgery, cellular and patient imaging and radiation equipment has been made possible by the foundation (table II).
The second avenue is directed at start-up financing for promising projects. In the past 6 years well over 100 projects have been supported by the foundation (table III), specifically directed at collaborative efforts bridging AMC and VUmc science and later on at junior researchers with promising concepts and PoC studies. To ensure that funds are spent wisely and allocated to academic high quality and high potential research an internal pre-clinical and clinical scientific committee judge applications. More recently, this process was further professionalized with the appointment of external chairs for the committees to limit potential conflicts of interest. In all, the foundation supported our institute with >25 million Euro (see table II,III) over the last 6 years and kick-started many research lines that went on to be successful in many competitive grant schemes, but is also a major investor in the new infrastructure.

Mission, vision and strategic priorities 2016-2022

Initial discussions within the institute clearly indicated that our research excelled in so-called translational chains where we cover the whole spectrum of fundamental to QoL research. The core value of Cancer Center Amsterdam at the start was therefore captured in the following phrase "Our research of today is the treatment of tomorrow" expressing the wish to excel at innovating treatment through research and the need to make impact through translation and through education of the next generation of researchers and clinicians. The complete text of the original mission and vision document can be found here and is summarized below.

Mission

As cancer is the leading cause of death in the Western world and remains a growing medical and socio-economic problem, it is our mission to provide the best possible care for cancer patients today and tomorrow. Innovation through excellent patient-centered research, through generation of relevant biological insight and diagnostic tools is at the core of our mission, along with a strong commitment to educate the next generation of clinicians and researchers.

Vision

It is our conviction that by joining forces we can become an international leading cancer center that is aimed at improving cancer therapy, life expectancy and quality of life for patients with cancer by focusing on (early) detection of cancer and to provide an optimal personalized treatment that builds on biological and clinical insight.
We share the belief that an integrated, multidisciplinary approach is necessary for the best and most innovative care, but also to bring findings from the laboratory into clinical practice. The cancer center will facilitate its excellent researchers in accomplishing these translational goals and will provide the best training of the next generation of students, doctors, nurses and researchers, paying attention to the latest developments in the field of oncology.

The strategy the cancer center set out to achieve the goals is therefore centered around a number of important pillars that form the foundation to excel in translational research. These are

- Integrate
- Facilitate
- Translate
- Educate

Based on these pillars 6 major priorities were set for the first years

1. Building research programs and themes.

The first and foremost goal of the institute was to create all-inclusive research programs that would encompass the width of our research endeavors. Aligning and integrating researchers in the institute and defining collaborative goals.

2. Branding Cancer Center Amsterdam and its researchers.

Although multiple interactions between our two units were already in place, it was important to realize that at the start a lot of our researchers and even the directorate itself were/was not aware of the full span of our cancer center. Identifying our researchers and *integration* of our two research centers was therefore the main aim at the initiation of Cancer Center Amsterdam trying to be all inclusive rather than selective.

3. Provide means to connect.

To further connect our scientists and to *facilitate* integration Cancer Center Amsterdam set out to organize PI meetings, seminars, topical meetings and large retreats. In addition, the cancer center made a strategic decision to invest most of its budget into *facilities* where scientists would meet and interact.

4. Building a community by providing peer to peer support.

Next to facilities, strategic investments were made in joined start-up proposals and into integration of research programs to spur interactions, all with a focus on research that could be linked to our *translational* goals. Combined with the foundation of joined scientific committees to judge proposals, and peer to peer support on grant writing, this was directed at *facilitating* our research efforts and enticing further interaction between our researchers.

5. Translation of novel insight.

The goal was set to innovate care and hence to drive pre-clinical (biological and immunological) insight into clinical trials. Cancer Center Amsterdam therefore focused on obtaining clinically relevant insight into disease progression, resistance mechanisms and diagnostic tools with a goal to translate.

6. Providing education to our upcoming talent.

Realizing that innovation requires talent and that PhD candidates represent the largest group within the cancer center with a wealth of talent, *education* of our PhDs through an excellent graduate school was incorporated in our goals.

During the first 4 years of Cancer Center Amsterdam the plan to formally merge both AMC and VUmc gradually started to take form and in 2018 contracts were signed. The merger meant that clinical departments were aligned and lateralized within the larger Amsterdam UMC. The current situation is that all clinical departments have merged into one and several have physically moved to one of the two hospital locations (location AMC or VUmc). As a result in a few years the complete oncological domain will be housed at location VUmc (2025) and this provides the foundation for the next steps in our strategy, which is to integrate oncological care with our science. Optimization of the interaction between scientists and caretakers, but also the regional expansion of our research will strengthen our focus on translational science even further. The mission/vision of cancer Center Amsterdam was therefore also extended to include care and as a result during the second phase, all strategic priorities that were set for the first phase were still highly relevant, but 4 additional priorities came into play.

7. Patient research groups.

Our research programs were defined according to topics rather than tumor types, which helped building our network organization and provided a perfect platform to integrate scientific efforts and to invest in our programs (see section “Evidence”). Nevertheless, our key strengths were in part aligned with translational chains that centered around specific tumor types. To incorporate these translational chains, emphasis was given to so called patient research groups (PRGs), which will be a crucial part of the program clinical therapy and supportive care, with the prospect to integrate pre-clinical (biological) insight into clinical research and vice-versa.

8. Regional, (inter)national collaboration.

The size of our cancer center, but also its regional role in cancer care comes with the obligation to look beyond our walls and incorporate science into a more comprehensive context. This is both an obligation as well as a necessity as for some of the diagnoses (part of) the cancer patient’s therapy occurs in regional centers and for both pre-clinical and clinical research the connection with the patient is of utmost importance. Similarly, high complex low volume studies require multicenter collaborations often in an international context to reach sufficient patients. Translational oncology therefore goes beyond the borders of Cancer Center Amsterdam.

9. Investing in local merger of Cancer Center Amsterdam.

The physical relocation of many of our researchers to the location VUmc combined with the ageing building in which most of our VUmc researchers were housed resulted in a strategic investment of Amsterdam UMC together with Cancer Center Amsterdam’s private partners into the so called research and diagnostic center (RDC). This new building, which is currently arising at location VUmc, will house most of our pre-clinical research as well as the pathology and human genetics departments. Cancer Center Amsterdam made a strategic decision to create research hub with centralized facilities and meeting space to inspire and facilitate.

10. Business development and grant support.

Despite a continuous need for innovation of cancer care, the center has seen an increasing competition for funding. To facilitate our scientists, Cancer Center Amsterdam invested in dedicated business development as well as grant support. Professionals were appointed to open up new avenues of funding either through collaboration with industry partners or through novel granting schemes.

Strategy (including the strategic process)

Cancer Center Amsterdam defined itself as a translational cancer institute with excellent preclinical teams that foster the development of novel diagnostic and therapeutic options through biological insight. In addition, the presence of world-leading clinical research teams in a large number of oncological domains varying from tumor-specific areas to specialties, such as surgery, radiotherapy, hematology and medical oncology, set the scene for the initiation of specific programs that incorporate the full extent of our research. The choice for broad programs was therefore a strategic step towards full integration of all our scientists. These programs were further subdivided into themes that still had a relatively broad nature (see appendix 1). Importantly, the programs and themes were intended to facilitate interaction and hence were never intended to be restrictive. Most of our researchers therefore find a place for their research in multiple themes and this is encouraged as we believe that innovation cannot be restricted and often depends on multidisciplinary interaction. The strategy set by the themes is designed and executed by theme leaders who together with the two directors have a seat in the research board where strategy is discussed. In addition, the research board controls the investments of the institute and research board members all deal with one or more portfolios (table I). Investments into these portfolios is decided on by the research board and organized together with dedicated staff (see below and table II and IV).

Program 1. Cancer Biology and Immunology

This program encompasses a large fraction of our fundamental and preclinical research and is divided into 3 themes being; Cancer Biology, Cancer Immunology and Target & Therapy Development.

Cancer Biology's strategy is to innovate through biological understanding of the events that lead to cancer initiation, progression and therapy resistance. The detailed analysis of relevant tumor models *in vitro* and *in vivo*, the use of and link back to patient material is at the core of this program. Understanding the heterogeneity between patients and within tumors, the intricate cellular interactions that take place in cancers and the pathways and perturbations that lead to cancer are all addressed within this program. Large tumor domains include GI cancers, hematological malignancies as well as head and neck cancers.

Cancer Immunology's strategy is to accelerate the discovery and development of innovative immunotherapies to further revolutionize cancer treatment and improve patient outcomes. To achieve this mission, the theme bundles all cancer-immunological expertise and as such is a shared domain with the Amsterdam Infection & Immunology research institute. The cancer immunology theme invests in facilitating collaboration between scientists, clinicians, and industry partners to boost new discoveries and to introduce new treatments for patients. Moreover, the theme believes that bundling of expertise and standardizing immune monitoring with dedicated facilities is of importance to translate findings to the clinic.

Target & Therapy Development reflects the strong translational research signature of the cancer center, bringing together therapy-oriented researchers that form the 'translational' bridge between biological insight and therapy development. The theme aims to provide a platform for fruitful collaborations and exchange of expertise, technology and new developments. Through descriptive and functional genomics approaches and screens and molecular and functional analysis of signaling pathways, novel therapeutic targets will be identified. Chemical and biological inhibitors of candidate targets are tested in a preclinical setting, employing cell lines, but essentially also relevant models of primary patient material (organoids and xenografts), as well as transgenic animal models.

Strategic investments

Within the program Cancer Biology and Immunology the cancer center invested into facilities, key equipment and the organization of expertise centers.

- CRISPR expertise Center (appendix 3) was founded to facilitate the implementation of this rapidly evolving technology into our research. Expertise on developments and compilation of protocols and tools, such as libraries, has made a significant impact on the research within this program, but also beyond the cancer center as this expertise center is providing support even beyond our national borders.
- The Immunotherapy Center (appendix 4), which aims to centralize and standardize immune monitoring in cancer and bridging basic immunological insight with clinical expertise. The appointment of a coordinator is directed at aligning the multitude of research projects and to enhance visibility.

- The cancer center invested in high end equipment such as the Hyperion (appendix 4), an imaging mass cytometer, to facilitate analysis of tumor samples with ~30 proteins at the time. This allows for spatial resolution of immune, stromal and tumor cell populations and provides innovative insight into (immune) regulatory circuits in cancer.
- Investments in different imaging equipment, including a FACSorter, confocal microscopes and an Incucyte allows for further image-based studies on biology, immune analysis and drug development (See table II, IV).

Program 2. Imaging & Biomarkers

This program encompasses the research in the development and translation of prognostic/predictive biomarkers and imaging techniques to support precision medicine. It is subdivided in an Imaging theme and a theme focusing on molecular Biomarkers.

Imaging's strategy is to develop and implement new imaging technologies and methodologies, including the use of quantitative imaging biomarkers, for improved personalized patient care and research. Practically, this implies that the theme plans to develop new and more specific radiotracers, MRI sequences and image analysis methods, including radiomics and artificial intelligence. *Imaging* seeks new insights by combining medical imaging data with data from other disciplines. The enormous investment of Amsterdam UMC into centralization of all imaging modalities in the hypermodern imaging facility (appendix 5), which was opened at the end of 2019, allows for an absolute state-of-the-art imaging of patients for research and care. The center incorporates a Tracer GMP laboratory and 4 cyclotrons and is thus at the fore-front of imaging development.

Biomarkers' strategy is to exploit the unique features of molecular biomarkers to cover essentially all aspects of cancer care from early detection and tissue-based prognostication to blood-based disease monitoring and therapy outcome prediction of individual patients. The principal strategy was initially aimed at connecting experts at AMC and VUmc locations that are engaged in biomarker research and to exchange expertise in innovative technologies, methodologies and patient (sample) cohorts. Aware of the increasing trend of biofluid-based biomarkers, strategic decisions were made to invest in the liquid biopsy space, coupling of clinicians' interested in biomarker development with the expertise of the theme.

Strategic investments

In the Imaging & Biomarkers program, Cancer Center Amsterdam invested strongly into facilities and equipment to enhance the potential of liquid biopsies as well as novel imaging modalities.

-The Liquid biopsy center (LBC) (appendix 6,21) is a unique enterprise where a multitude of biobanks, collecting different types of bodily fluid are being stored. Supported by the initial strategic investments of the stichting CCA and further support by the cancer center, standardized biobanking of biofluids of essentially all cancer indications are initiated and currently 11 active biobanks are in place with longitudinal sampling and world-class expertise in various methodologies including tumor-educated platelets, circulating tumor DNA and exosomes.

-Within the ADORE initiative, which has the vision to align oncology and neurology research on the Boelelaan Campus (see page 24 and appendix 7) a total body PET-CT (appendix 8) was acquired that has lifted our potential of in patient imaging to an absolute world-leading level. Due to enhanced sensitivity and resolution time lapse imaging is feasible, but more important specificity of imaging is enhanced dramatically allowing for the analysis of drug delivery and in the future, ATMP circulation.

-Gallium68 generators (appendix 8) were acquired and are currently operational. The first Ga-labelled tracers have been generated and applied for clinical research. The availability of this system allows for relatively rapid in house development of tracers.

Program 3. Cancer Treatment & Quality of Life

This program entails the major part of our clinical research and has a very broad range. It encompasses amongst others surgery, internal medicine and Radiotherapy-based trials and extends towards research that aspires to improve on QoL. Importantly, there is a very high multidisciplinary character to this program, which is related to the increasing complexity of cancer care and innovation. Originally this program was split into 3 themes, but quickly adapted to 2 themes as this created a more logical division between research areas. The two themes are Therapy and Supportive Care.

Therapy's strategy is aimed at creating multidisciplinary teams that strive to take a leading role in improving cancer therapy. As this theme includes all primary medical specialties involved with direct patient treatment, but also supporting medical specialties and state-of-the art expertise on quality of life, building research groups centered around patients and tumor types is key. Within the clinical domain the majority of research projects center around gastrointestinal cancers and second hematological malignancies where major (inter)national trials are conducted from within the theme. Other similarly active tumor domains are lung, head and neck, brain, gynaecology, urology cancers but also some rare cancers. To accommodate all efforts building (regional and national) platforms and learning from other disciplines to achieve better interventions is a strategic decision made by this theme.

Supportive Care's strategy is developed based on the fact that, although cancer patients are living longer, they still carry the consequences of their disease and/or treatment, and a relevant proportion still dies from the disease. Therefore the strategy is geared towards research into prevention and treatment of symptoms and side-effects as an essential part of cancer care. This part of care, broadly referred to as supportive care, includes physical and functional, psychological, social and spiritual well-being. Although still a relatively young field the scientific evidence for the benefit of supportive care is expanding and envisions to generate more evidence-based interventions and implement currently proven interventions. Importantly, supportive care is multi-dimensional and multidisciplinary with experts from a variety of fields (e.g. nurses, clinicians, pastoral workers or physiotherapists) involved in this care and the theme incorporates all these various types of researchers.

Strategic investments

Within the program Clinical Therapy and QoL Cancer Center Amsterdam invested into aligning efforts into clinical studies and into facilities that benefit clinical studies. Some of these investments are mentioned above, like LBC and total body PET-CT, which enhance our capacity to perform innovative trials. Other investments are

-Proof of Concept studies (appendix 9), which are a key first step in translation. This investment is still relatively small but marks a step towards translation of our own research, which was set as a criterium for funding. This investment also builds on peer-to-peer support to acquire competitive funding for PoC studies.

-Amsterdam Clinical Research Support. This investment is crucial for the continuation of success of program 3. Right from the start of Cancer Center Amsterdam, an investment was made to first archive all clinical research units involved in the design and execution of investigator-initiated and industry-sponsored clinical trials. This led to the next step done within the ADORE initiative in which a dedicated unit is being formed that brings together all knowledge on (innovative) trial design, legal and financial questions and the actual execution. All to facilitate our researchers in their clinical trial ambitions.

-CCA-APP (appendix 10). Investment into the use of digital platforms to perform online measurements of patient characteristics. The use of data collection and patient reported outcome with home-based devices such as Fitbit and smartphone apps allows for continuous monitoring. The platform was initiated to study whether ambulatory monitoring of patients receiving immune checkpoint inhibitors would be beneficial.

Integrate, Facilitate, Translate and Educate

Overall the cancer center designed and used its strategy to *integrate* all cancer-related research within Amsterdam UMC and to *facilitate* its *translational* program. The design of the programs and inclusion of researchers within the different themes was purely based on fitness rather than being restrictive on quality, thereby building a large network organization. In addition, Cancer Center Amsterdam invested in branding of the complete cancer center by providing a website (www.cancercenteramsterdam.nl) with information on our researchers, appointing a communications officer and by professional newsletters and yearly reports (2022, 2021, 2020, 2019, 2018, 2017), all with the goal to familiarize our researchers and the outside world with Cancer Center Amsterdam.

On top of this we set the strategic goal to organize as much interaction as possible to provide the means to connect. A yearly retreat is organized (~400 participants), which allowed for exposure of our researchers to the full spectrum of research and to discuss collaborative innovative goals and means to make each other stronger. Multiple seminar series (CCA-Next and CCAll) were initiated and topical seminars and symposia were organized by our different themes.

In line with the wish to *integrate and facilitate*, the strategic investments described above were made. The cancer center's board believes that by broadly facilitating the network organization the biggest impact can be made. At the

same time, the yearly investments of the Stichting CCA into the cancer center were used to initiate a project call for our (young) PIs with collaborative, start-up initiatives (~1,5 million/year) (table III). The push towards *translation* was already at the core of our institute, but was further highlighted by these yearly calls for project funding, which were evaluated on quality, collaboration, but also potential for *translation*. Similarly, the initiation of a call for PoC trials in 2022, where *translation* of our own preclinical findings was the main criterium, further strengthened this strategy. Next to a direct stimulation of our scientists, this initiative was aligned with the formation of scientific committees and peer-to-peer support. Especially the latter improved quality of our research, resulted in targeted *education* for our young scientists and as a bonus *connection* between our scientists.

Last but not least, the cancer center aligned its educational efforts with OOA, a graduate school with a solid history that provides a platform for oncological PhDs in Amsterdam. Uniform standards for graduation were set and the school provided topical educational courses and PhD retreats (appendix 2). In addition, next to the project call described above Cancer Center Amsterdam invested in young PIs, first by identifying our talent and second by helping them in acquiring funds for their research.

Restructuring theme leadership and midterm evaluation

The different themes were at the start headed and organized by 4 theme leaders per theme to allow for maximal exposure, network formation and division of labor. Although this worked very well to integrate research, it also resulted in a rather convoluted team of leaders and responsibilities. In 2020 we therefore restructured the programs and theme leadership and appointed one leader per theme (picture 4) who is responsible for the organization of the theme and the creation of a core group of researchers that would serve as ambassadors for the theme. Core responsibilities of the theme leaders, who still hold a seat in the research board, did not change.

Midterm review

Based on the first years a self-evaluation of the institute was made and a midterm review with internal auditors was performed. Strengths were considered to be our large community that harbors a lot of talent both at the senior and junior level and the execution plus often leadership in large impactful clinical trials. The size of the institute, when used properly is a clear strength as it allows for shared investments that benefit all our research. In contrast, the lack of dedicated research time for clinicians, the diversity of the institute in terms of location/departments and type of research are regarded our weak points. Not surprisingly, Cancer Center Amsterdam therefore emphasized the need to integrate, as concentration of our research is by far our biggest opportunity. Together with the novel infrastructure, but also with an eye for translational chains and in connection with our partners Cancer Center Amsterdam can grow. It is also evident that we will have to consider certain threats. First our researchers have their primary affiliation with a department and need to be attracted to fully integrate into the cancer center. More external threats are the complexity of a. funding, which is increasing with more consortia-based programs, b. clinical trial regulations and c. rules around interaction with commercial partners. Better and more (legal) expertise is needed to negate these threats.

The midterm site visit further revealed that Cancer Center Amsterdam should try to organize talent support better and to address the funding opportunities. In addition, cohesion within the institute and between programs required continued attention. Finally, the site visit committee suggested to visualize the actual financial input into research (competitive funding plus institutional funding including staff salaries) and to make the translational efforts quantifiable. As a result we have appointed a grant support officer (appendix 11) and invested in business development to attract more funds (appendix 12). In addition, we have invested strongly in web-based tools to measure our scientific and societal output as well as our translational impact (see page 14, Evidence). Talent support is in part organized from within the institute, but is also structured through the larger Amsterdam UMC community and this remains a point of attention. We did start dedicated grant support and internal rounds for funding for young PIs. Finally, cohesion we believe is a continuous mission of Cancer Center Amsterdam and based on our analysis one that we are successful at as a strongly integrated publication network is evident between our principle investigators and is becoming stronger over time (appendix 13).

Evidence

The formulation of a number of strategic aims has helped the cancer center to achieve several of its original goals. For instance, establishing programs has resulted in integration, while strategic investments have resulted in a strong incentive for our translational research and promoted interaction, thereby further facilitating the alliance. The evidence provided for this can first be derived from a full analysis of our publication output. A total of 6744 referred articles were (co-)authored by our scientists (manually curated to only include cancer-related publications from an original of more than 10000 publications). Using these publications, an interaction-based analysis was performed by the Centre for Science and Technology Studies (CWTS) and projected in VOSviewer (van Eck and Waltman 2010). This indicated that 4 big clusters of associated publications are visible within our dataset (Figure 4, upper right; red, green, blue and yellow). More importantly, when we analyzed the publications of the three programs and projected these onto this map, clear support for our choice for 3 programs emerged (Figure 4, lower 3 panels and Online). Indeed, yellow highlighting of the publications per program and subsequent projection onto this map revealed large clouds of publications in the Cancer Biology & Immunology and Imaging & Biomarkers programs overlapping strongly with one cluster (green with CB&I, blue with I&B), suggesting that all publications within these programs are highly interrelated in topic. Clinical therapy & QoL was a bit more diverse with a large QoL cloud, plus a local and a systemic therapy cloud, but still revealed strong clustering (Figure 4). Of course the interaction maps also show extensive connections between the clouds, but we feel that this analysis supports our strategic choice to build topical programs where projects find common ground.

	Cancer Center Amsterdam					
	Total*					
	2017	2018	2019	2020	2021	2022
Refereed articles	1048	1098	1127	1092	1276	1103
Non-refereed articles	34	30	36	41	79	46
rest	32	23	28	27	49	11
PhD theses	82	69	74	95	99	87

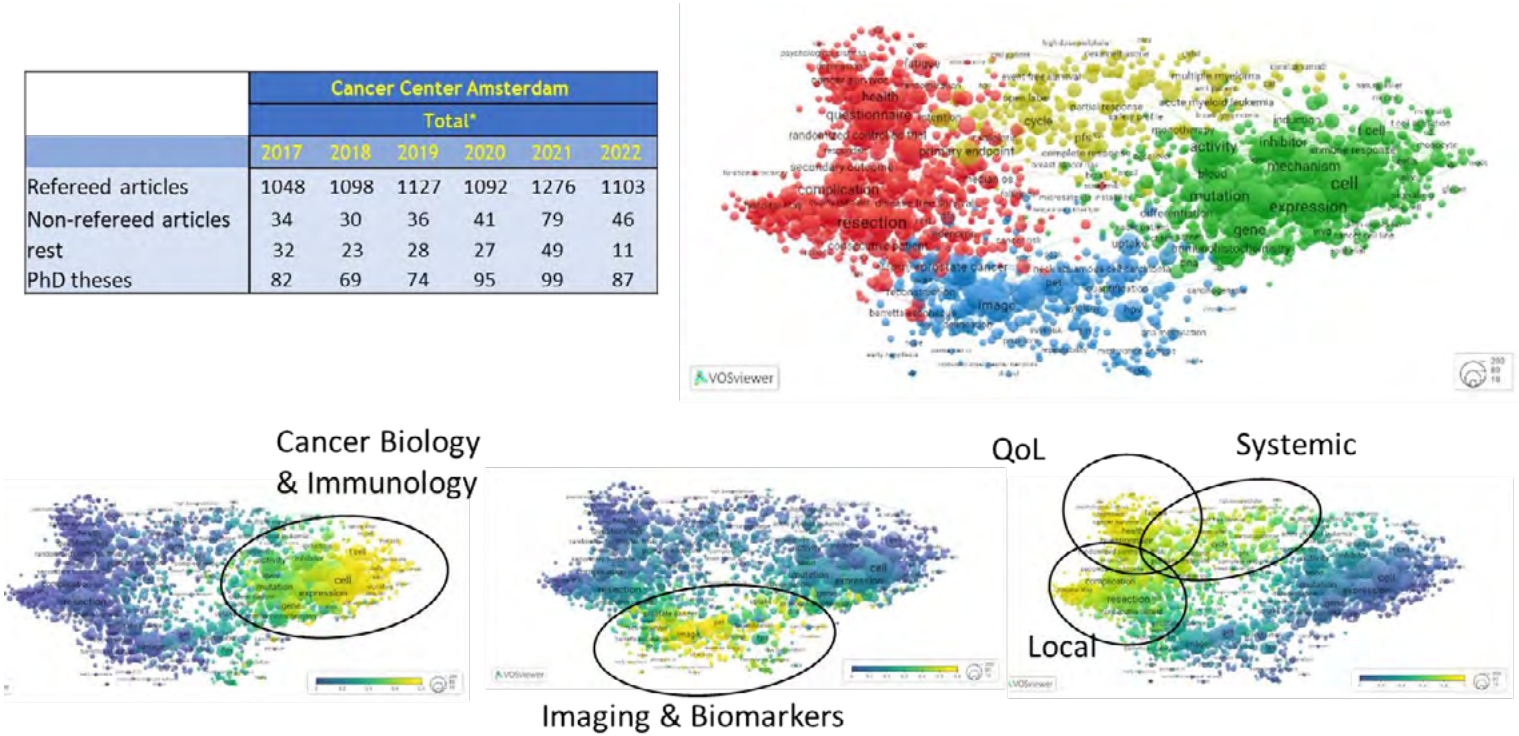


Figure 4. Table of output of Cancer Center Amsterdam in numbers per year and VOS viewer representation of all publications of Cancer Center Amsterdam. Connections are based on keywords and interaction terms and show large associated domains (Green, blue, yellow, red). Of note, color coding of the fraction of publications that fall within the 3 programs indicate that these strongly associate with the different clusters. (Green is Cancer Biology & Immunology, blue is Imaging & Biomarkers and red/yellow is Therapy and QoL). Further subdivision of the third program is shown for local, systemic and QoL publications, which is an estimation based on the terms that show up in these clusters.

Next to the interaction analysis, we also analyzed our publication output by identifying interest to domains such as industry, hospital care, clinical guidelines, policy documents, media and patents (appendix 14). These analyses reveal strong affinity of the different programs with specific clinical, societal or industry interest. Although these analyses are of interest, they are based on keywords and terms used in our publications and the associated interest in these keywords in the

different domains. These measure thus mainly provide insight into the potential of our work to be relevant for the different parties rather than their actual use. To achieve a more direct measure of our impact, we co-created a novel evaluation tool together with the Research Intelligence team of the Vrije Universiteit Amsterdam. This so called research dashboard incorporates world-wide publication records of large cancer centers to whom we like to be bench-marked (appendix 16). Publications are incorporated based on publication (mesh) terms and categorized by tumor-type, by institute, by research domain and can be analyzed by citations, impact and by collaboration. Importantly, we have extended this database using an analysis of all these publications in relation to their use in policy documents from sources like EMA, WHO, FDA. The web-based tool we developed is available for our researchers and the committee (research dashboard) and contains >116k publications from 21 (cancer) centers world-wide (2016-22). Several observations stand out from the analysis with this dashboard. First, we are within the top in size, i.e. very productive, when it comes to our Gastroinstestinal Oncology research program and specifically upper and lower-GI rank very high. This is even more so, when clinical trial-based studies are evaluated (Figure 5). In addition, albeit still small we are also very strong in the rare cancer Retinoblastoma.

When analyzing an average impact it is clear that specifically hemato-oncology and Neurooncology score high in relation to peers world-wide and even more so when hemato-oncology was selected for clinical trial related publications (Figure 6). Both also rank second of these institutes when analyzing average number of citations.

The use of this research dashboard combined with an analysis of the input (table V) provides highly usefull insight into the domains that are excellent, large, small or in need of attention and are currently used to discuss strategic options for the respective domains.

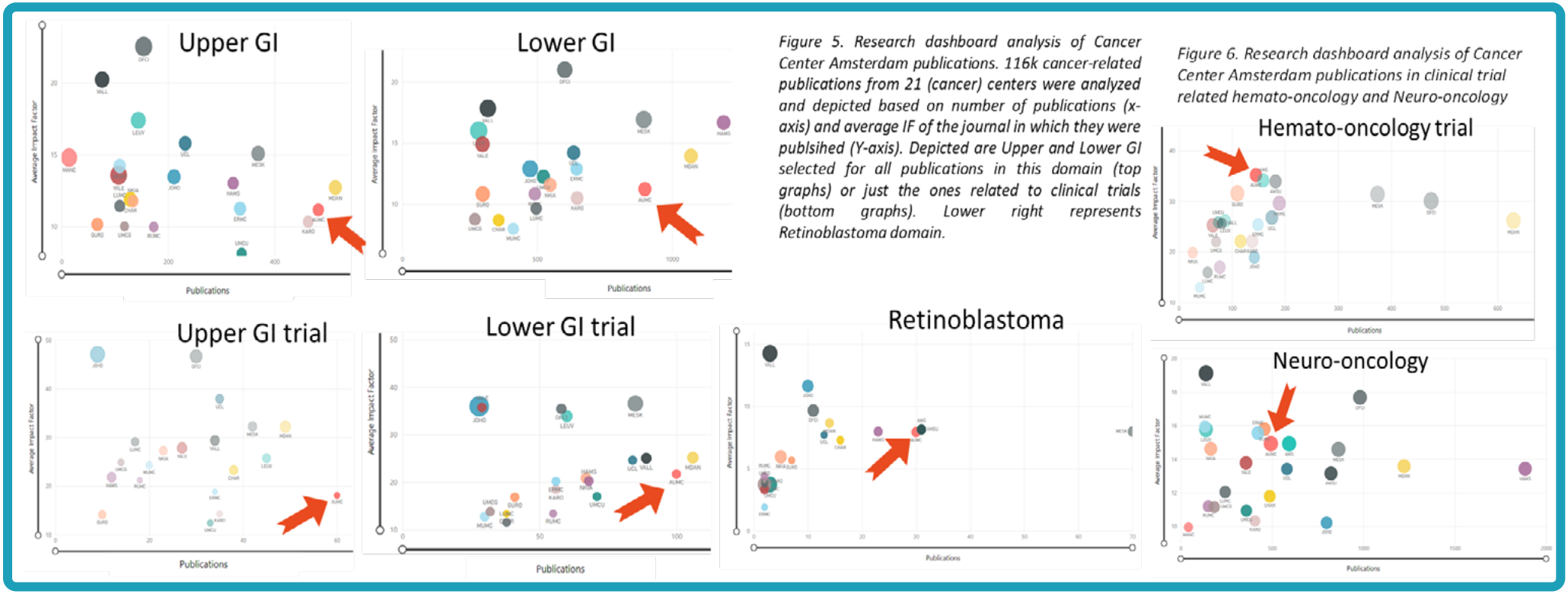


Figure 5. Research dashboard analysis of Cancer Center Amsterdam publications. 116k cancer-related publications from 21 (cancer) centers were analyzed and depicted based on number of publications (x-axis) and average IF of the journal in which they were publsihed (Y-axis). Depicted are Upper and Lower GI selected for all publications in this domain (top graphs) or just the ones related to clinical trials (bottom graphs). Lower right represents Retinoblastoma domain.

Figure 6. Research dashboard analysis of Cancer Center Amsterdam publications in clinical trial related hemato-oncology and Neuro-oncology

Research quality (Table)

Research products for peers

The research output and PhD graduations of Cancer Center Amsterdam are summarized in table VI. A total of 6744 publications, excluding book chapters and conference proceedings, were published by our researchers and these are distributed roughly in a 1:0,8:2,5 ratio across the 3 programs with the notion that there is extensive overlap. The output of our work is to a large extent collaborative, either within the cancer center or with (inter)national partners.

A total of 506 PhDs successfully defended their thesis and graduated within Cancer Center Amsterdam and under guidance of our graduate school (table VI). Currently we have over 550 PhD candidates in our center and on average the time to graduation is 5,6 years (appendix 2 and page 20).

Importantly, several (multicenter) clinical studies were executed in the past years within Cancer Center Amsterdam, the outcome of which forms the basis for changes in the standard-of-care. A selection of these game-changing clinical studies is given in table VII.

Finally, the R2 bioinformatic platform, which is a web-based analysis tool available to researchers world-wide (appendix 15), was extended in terms of number of datasets, users and tools provided to the users. Moreover, we established a Liquid Biopsy platform for a larger community and have established a world-class imaging center that is open for collaborative efforts.

Use of research products by peers

The work we have published in 2017-2022 is to date cited more than 100.000 times, which means an average of >15 per study. Importantly, the percentage of non-cited work in the period 2017-20 is less than 3,5% (table XIII). Several key studies made an enormous impact and have been used extensively by our peers. For instance our top 25 publications in terms of citations have on average well over 700 citations per article. The analysis performed by CWTS further indicates that our work is cited much more frequently than the world average and this number is also rising) (MNCS2017-19 =2,02/MNCS2019-22 = 2,28). This is a measure of our impact, but in a way also an obligation for the position we aspire to have. Our own research dashboard provides more detailed insight into the specific domains that receive above average citations. Hemato and Neuro-oncology research are two domains worth mentioning in this context that receive relative high citations (Figure 6).

Next to the primary publications, our scientists have also authored/contributed to a number of excellent reviews and nomenclature papers, which are extensively cited by peers. The top 10 of these received over 10000 citations in the last 6 years.

Finally, our R2 platform, in which Cancer Center Amsterdam invested, has more than 9000 registered users and has served 194.000 ip addresses world-wide and hosts a total of ~4000 datasets and a current staggering >100.000 sessions/year (appendix 15). The same holds for our younger CRISPR platform that not only serves internal clients but also receives requests from external teams (appendix 3).

Recognition from peers

We are extremely proud of the recognition received by many of our institute's members (table VIII). Individual grants include 3 ERC consolidators, 4 ERC PoC grants, 11 national VENI, VIDI, VICI grants for talent at different stages of their career (5 VENI, 4 VIDI, 2 VICI, total 7.5 million euro). Our young talent was further awarded with 10 Young Investigator grants from the Dutch Cancer Society (~8 per year given). Next to individual grants, a total of 10 coordinatorships of Dutch Cancer Society consortium grants (total value 15 million), 2 EU and 4 Marie Curie project coordinatorships were acquired in the past years, while 27 teams participated in EU consortia. Last but not least, the prestigious Spinoza prize was awarded to Yvette van de Kooyk for her work on glycobiology in tumorimmunology.

4 of our PIs are also part of the ONCODE institute (total 50-60 PIs reside in ONCODE), a national cancer institute that selects fundamental cancer scientists based on excellence. Next to this a lot of our scientists held/hold leading positions in national and international societies, are member or chair of national and international scientific committees, including ERC, and are (associate) editor of scientific journals (table IX).

Relevance to society

As indicated by the midterm evaluation, defining the success of our translational and societal impact is complex. It is highly diverse in nature and ranges from changes in clinical practice, valorization of our knowledge through guideline committees, business development and implementation studies. However, with societal impact we also include the impact we make on the population at large, by for instance screening programs, but also patient meetings or public outreach. In addition, this involves, very directed programs to help patients cope with cancer that is based on our active research program in this area. Our use-cases (see next chapter) provides examples of key achievements, while the dashboard we developed helps us to quantify and benchmark the impact we made through policy documents.

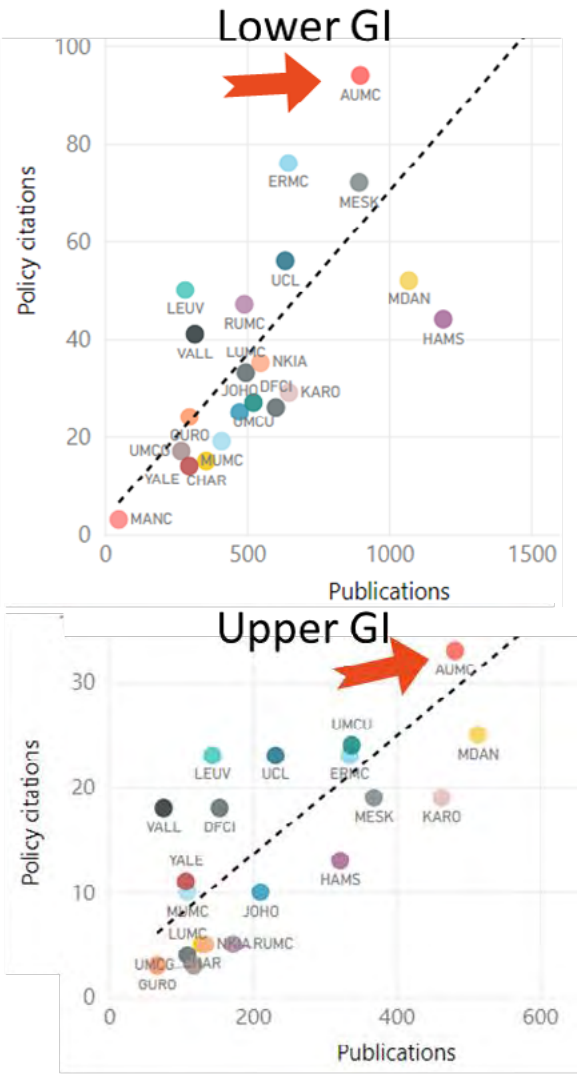


Figure 7. Research dashboard analysis of CCA publications and their use in policy documents. Database represents 1600 documents and 6500 citations. In lower GI 443 CCA citations are reported total of which 94 are authored by our researchers. In upper-GI this is 33 out of 167.

Figure 8. European mao of institutes with whom we have co-authored publications

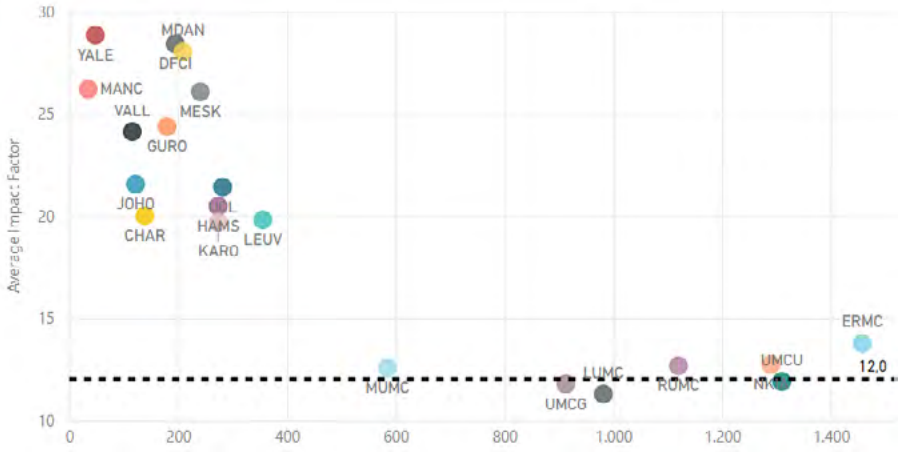


Figure 9. Analysis of collaboration on all Cancer Center Amsterdam publications with all other centers analyzed. X-axis shows numbers of shared publications, y-axis average impact factor.

Table

Metrics

Analysis of policy documents within our dashboard and specifically the use of scientific literature (citations) within these documents revealed that there is a world-leading position of Cancer Center Amsterdam in Upper and Lower-GI cancers, meaning none of the other institutes has more impact on these policy documents (Figure 7). Also for hepato-pancreato-biliary cancers we rank in the top of the institutes (appendix 16). Next to the impact of our work on policy documents, we also analyzed the collaborative maps of our science with the idea that world-wide collaboration also aids in the way we can distribute our science and make impact for society. In figure 8 a map of all collaborative institutes in western Europe is shown (appendix 17=world-wide), whereas figure 9 shows an interaction map of the publications in our dashboard and this provides interesting insight into our largest partners (ErasmusMC, UMCU and NKI-AvL), but also in the average impact of joined publications, which appears to be more prominent for the international collaborations. Beside these efforts we can measure the success of our business development activities where we strive to increase our impact by aligning with external partners (appendix 12).

Research products for societal target groups

In the past years we have made significant progress to involve patients and the public in our research. Most cancer domains have patient-information days that are often organized on a yearly basis (esophageal, pancreatic, Rb, Hematon, LYMMcare). Multiple PIs of Cancer Center Amsterdam have joined or organized national or local fundraising activities to inform the public about cancer research and to attract funds for research (Stand-Up to Cancer, Marathon of Amsterdam, Lymph & Co, Darm to Darm Ride). Important impact is also made by some of our leading PIs in the national screening programs for colorectal and cervical cancer and the HPV vaccination campaign both in informing public about the programs as well as in scientific projects involving the screenings programs. More individually, we are proud of one of our immunology PIs who has been a central figure in explaining COVID-related immunology on national news, but has also invested in a book to inform the public about cancer. Others have been invited to showcase their work to the Bill & Melinda Gates foundation or to patient groups.

Next to this, several efforts have been made to link our research on QoL with the patient population and to provide means to support patients to cope with the disease and the treatment. One big example is Oncokompas, which is a web-based self-management instrument that allows for QoL monitoring by patients and/or partners. Close to 4000 patients have used this tool and do so repeatedly during a 6 month study period. Another is the work and implementation of shared-decision making tools. In addition, we have some very exiting societal impact parameters that are based on Cancer Center Amsterdam studies that show the benefit of art to improve QoL. These arts' projects include a theater project for and by adolescent and young adults with cancer called "Staging Cancer" and an exhibit in Amsterdam UMC of art made in co-creation between artists and patients called "In search of stories".

Use of products by societal target groups

The use of some of our products is measured directly by followers or website visitors. Our LinkedIn profile, our website (Cancer Center Amsterdam and Amsterdam UMC) as well as some of the more local Instagram accounts are used frequently by a variety of professional and public followers. The same holds for an expanding group of followers that receive our yearly reports of Stichting CCA and Cancer Center Amsterdam. We also organize multiple meetings a year for our sponsors that are visited by many of these supporters.

Some of our products are used directly by industry partners an overview of these is given in appendix 12.

Besides the external users, our Cancer Center Amsterdam researchers co-organize multiple courses for the graduate school that serve PhDs from our cancer center but also from NKI-AvL. The exact numbers of PhD candidates we serve with these courses can be found in appendix 2.

Accomplishments, research quality and societal impact

Cancer Center Amsterdam has had a highly successful 6 years in which the strategy to integrate, facilitate, translate and educate has proven to result in a strong institute that is now almost completely housed at one location. The institute encompasses ~140 full professors, ~100 assistant/associate professors, well over 150 postdoctoral researchers and currently nearly 600 PhD candidates (table X). Although there are still a lot of steps to take to fully integrate care with science, the direction is clear and embraced by the organization. Below we would like to highlight a number of accomplishments that we believe exemplify our efforts and achievements. In line with the proposed order in the evaluation protocol we include our achievements on open science, academic culture, HR and PhD education.

Open Science

As Cancer Center Amsterdam is not a direct employer we have an advisory role in the use of open science sources. It is evident that both Amsterdam UMC and Cancer Center Amsterdam strive for full open access (OA) publishing and data sharing. Through the installation of open access contracts with publishers researchers can publish OA via the golden route free of charge in more than 10.000 journals. Support and information regarding OA publishing is provided by the Medical Library for UvA and by the UBVU. In table XI one can see that this policy is paying off and Cancer Center Amsterdam sees an increasing percentage of Gold OA over the years (83% in 2020). This percentage rises even further when just first and last authorships are regarded, suggesting that our researchers indeed strive to publish OA. Next to the information provided by the libraries, we actively advertise these options at our PI meetings.

For the reuse of data, it is a prerequisite that research data is stored in a Findable, Accessible, Interoperable and Reusable (FAIR) way. Amsterdam UMC provides FAIR data options through the Research Data Management department, which facilitates the creation of FAIR datasets by providing researchers the tools and support for drawing up Data Management Plans. Amsterdam UMC researchers can use the open data repository DataverseNL to share metadata and publish their research FAIR data sets, open or under conditions for reuse. Cancer Center Amsterdam itself invested specifically in data sharing through its R2 platform and supported the in house developed FigLinq. The first allows users to share and navigate (gen)omics data in a user friendly manner, while the latter is a platform for management, analysis, visualization and publishing of data in which the primary data remains accessible and can be made fully open access to allow reuse and re-evaluation by third parties. Both provide valuable options for data sharing by our researchers (appendix 15). Finally, all data from our proteome facility is shared via proteomeXchange and scripts are available through oncoproteomics.nl. Phosphoproteome analysis can be uploaded in the INKA platform, which is made available through inkascore.org. and used for well over 500 analysis already.

Academic culture

Cancer Center Amsterdam promotes an open and academic culture in which the academic debate can flourish. We position ourselves as an institute in which we strive to conduct translational research, acknowledging the fact that we have a major task in educating the next generation of scientists and clinicians. The open academic culture is central in this training and enticed during local work discussions, institute seminars, retreats and conferences organized by Cancer Center Amsterdam. As employer, also Amsterdam UMC takes measures to ensure openness, (social) safety, inclusivity and research integrity and has web-based mandatory e-learning for all employees on this topic to increase awareness. The office of the ombudsman is responsible for the social safety policy and if necessary has a complaints procedure if discussions arise on misconduct. This office aims to improve social safety and to combat unethical and/or undesirable behavior, to increase ownership and responsibility of employees and managers regarding safety signals and to promote an open reporting culture.

Cancer Center Amsterdam endorses the Research Code that was developed by the Amsterdam Research Board and is an extension and local specification of the Netherlands code of conduct for research integrity. Importantly, all our starting PhDs are obliged to follow the course research integrity and we try to create an open atmosphere that allows for discussion on research integrity, acknowledging that ethics discussion change over time (i.e. the use of AI in research reporting with the advent of platforms like ChatGPT). To safeguard research integrity the

board of directors have appointed several independent confidants, who focus on research integrity. These counsellors can mediate and advise on complaints. Furthermore, they can have a role in the submission of a formal complaint to the research integrity committees, that are established by the Executive Boards of the UvA and Vrije Universiteit Amsterdam. The counsellors also report on a yearly basis to the Amsterdam Research Board on their findings. Most of these measures are required when the academic, open and inclusive culture fails. It is our ambition to negate the need for these structures, by a continuous emphasis on openness. Due to a high diversity in cultural background, especially in our population of PhD candidates (see below), and a realization that dependencies and unequal power structures exist, we do believe though that this requires continuous attention and discuss this at conferences and PI meetings.

HR

Cancer Center Amsterdam incorporates 38 departments and 9 divisions within Amsterdam UMC. As mentioned, the institute is a network organization and as such has no direct mandate in appointing its researchers, which are all staff, employed by the different departments. Hence, the cancer center follows and gives consent to the HR policy set by Amsterdam UMC, which is developing an active diversity and inclusion policy (for more details click here). This policy also includes the Commission Talent Amsterdam UMC, which evaluates proposals for promotion, but also features a mentoring program at all stages of the career. In addition, Amsterdam UMC has an overarching principle investigator (PI) system, which challenges individual researchers to take up leadership and gain visibility. PIs are appointed by the board of directors after evaluation by the Amsterdam Research Board (ARB). PIs should have a clear independent research line with at least one finished PhD mentorship and sufficient funding for the coming years. Cancer Center Amsterdam's scientific director plays a role in the appointment of PIs through the seat in the ARB. Moreover, the institute is consulted for the promotion of its staff to associated or full professorship. Every two years a plan is discussed for new professor positions, promotions and continuations with the deans and appointments require positive advice from the directors. In the past 6 years Cancer Center Amsterdam appointed a total of 18 associated and 40 full professors (table XII). Total numbers are quite stable over the years due to retirements/departures/promotions. Importantly, a clear diversity imbalance is evident within our professors, which we are trying to improve on by the appointment of more female professors than the current average. The cancer center does realize that this is still not sufficient and commits itself to a balanced gender ratio in 2035. This is a slow process, but the percentage of females rises gradually and especially the number of female PhD candidates is a sign that we do not lack talent. Of note, diversity beyond gender is also very unbalanced. Although we do have a lot of foreign PhD candidates, these hardly progress to staff levels. Moreover, cultural diversity is also limited and will need to be improved on especially at the level of professors.

Integrate, facilitate, translate

The institute is extremely proud of the successes that we have seen on integration.

-The yearly conference attracts more than 400 researchers from our institute and allows for an open atmosphere where the institute of origin of the attendants is no longer regarded. Ideas and collaborations are formed based on content rather than origin.

-The CCall seminars and PI meetings are visited by a clear mixture of scientists that is based on the topic of the presentation. Also here the steps we have taken to integrate science and to allow our own PIs from both centers to present themselves and their team have helped to build one network organization.

-The physical relocation of several clinical teams to location VUmc has resulted in joined planning of future structures and as such has really integrated departments. The same holds for the planning and now building of the research and diagnostics center (appendix 7) where we will house the vast majority of our laboratories, combined with a number of facilities (CRISPR, Genomics,

Picture 5. Impressions of OOA retreats.

Proteomics, GMP, Immunohistochemistry, screening, bioinformatics, iPSC) will finalize the integration and is planned to be completed in 2025.
-The OOA retreat and courses where our junior talents all meet, integrate and discuss science (Picture 5) is creating a sense of community.
-The building of programs and themes has helped tremendously in originally familiarizing scientists from both sites with the wealth of research within the themes, but also to build alliances. This was further spurred by the funding scheme within our yearly foundation call that supported alliance projects.
The translational signature of our cancer center is highlighted by key achievements in connecting our own (pre-)clinical research with the initiation of clinical trials. These involve the success of therapy in metastatic CRC (CAIRO studies), the neo-adjuvant therapy in esophageal and pancreatic cancer (PREOPANC), the combination therapies in CLL and the use of LiCl to influence intestinal stem cell competition. In appendix 18 several translational use-cases are described.

PHD policy, educate

As of 2022 the support of all PhD candidates of Amsterdam UMC is organized within one doctoral school, which is an extension of the AMC graduate school to both faculties. Importantly, the graduation of our PhDs follow the affiliation of our professors, which are associated to one of the two universities in Amsterdam. Hence graduation regulations have been slightly different between these two groups as the medical faculties have set different rules on top of the national requirements for a PhD promotion. Cancer Center Amsterdam has seemingly made this even more complex by the fact that we have our own graduate school (OOA) already in function for over 30 years. OOA houses both our oncological PhD candidates as well as those of NKI-AvL and this collaboration has proven to be very successful. Around a quarter of our PhD candidates are international and a total of 41 nationalities are represented within our PhD pool (20 European, 21 rest of the world). Despite the fact that we have two graduate schools, OOA has made the educational process more transparent for our oncological PhDs and together with the cancer center's board and the deans , OOA has aligned the PhD promotion regulations of both Universities and agreed on one set of educational rules for all its PhDs. Moreover, close collaboration with the Amsterdam UMC Doctoral School is in place to provide a comprehensive course program with topical courses (OOA) and soft skill courses (Doctoral School). In addition, a training and supervision program is mandatory for all PhDs, which describes the educational program (30 ECTs) as well as the supervision that will be in place during the PhD studies.
Next to the organization of the PhD program and its regulations, OOA organizes a very popular retreat, where PhDs meet, and has an active PhD council that advices OOA. Last but not least, OOA also invested in talent programs. First, by the initiation of the very successful Diamond program where master students were selected based on a competition and allowed to develop their own project ideas (appendix 19). Second, by organizing a Masterclass program for high school students with the goal to ignite enthusiasm for cancer research and attract the next generation of students. A separate self-evaluation of the OOA and its educational program for PhDs is given in appendix 2. The table below shows the most important data on the actual time to graduation of PhDs started in 2014 to 2018. Of note, this time to graduation is strongly influenced by . the waiting time till the defense and 2. The start of clinical training by clinical PhDs.

AmsterdamUMC		Graduation (#/%)							
Starting year	Total	In 4 years or earlier	In 5 years or earlier	In 6 years or earlier	In 7 years or earlier	In >7 years or earlier	Not yet finished	Discontinued	Other
2014	108	12 / 11%	24 / 22%	49 / 45%	72 / 67%	82 / 76%	10 / 9%	14 / 13%	2 / 2%
2015	96	10 / 10%	24 / 25%	41 / 43%	51 / 53%	65 / 68%	14 / 15%	17 / 17%	0 / 0%
2016	94	16 / 17%	34 / 36%	52 / 55%	61 / 65%		22 / 24%	11 / 11%	0 / 0%
2017	106	11 / 10%	24 / 23%	35 / 33%			62 / 58%	9 / 9%	0 / 0%
2018	107	17 / 16%	24 / 22%				83 / 78%	0 / 0%	0 / 0%
TOTAL	**511**	**66 / 13%**	**130 / 25%**						

Finally, Amsterdam UMC also houses the Association of Amsterdam UMC PhD Candidates (ASAP), which cooperates with the Doctoral School. They organize social events and are involved in organization and advice on the training of PhDs. They represent Amsterdam UMC PhD candidates in the Amsterdam Doctoral School Board and in national PhD candidate associations.

Program achievements

Program 1: This program is the largest when it comes to staffing with around 300 staff and 240 PhD candidates on average and has seen a strong output over the past years with more than 1600 publications total, of which ~90% is open access in the last years (table XIII). Average citations per paper are around 17 with a large number of publications that are cited more than 200 times (17x). Key achievements are the identification of active stem cell competition during intestinal transformation, mRNA expression based subtype identification in multiple epithelial cancers and the associated development of specific therapies and diagnostic tools. Moreover, within this program we saw the development and use of bispecific T cell engaging and neutrophil engaging antibodies, the use of CAR-T cells in hemato-oncology and the development in off-the-shelf CAR-T. Finally, within this program we developed the local use of CpG to modulate lymph node immunity in melanoma, the combinatorial use of Venetoclax and ibrutinib in CLL and we identified regulators of adhesion in hemato-oncology. Importantly, several of these projects are pushed forward to PoC studies or even larger clinical trials (table VII). Several use-cases that highlight the success of this program can be found in appendix 15,19&20 and include; a. the success of R2, b. the use of LiCl to prevent stem cell competition during transformation and c. the success of vaccination and combination therapy in hemato-oncology.
Next to the extensive output this program acquires between 11-14 million euro in external funding per year (table V) and is especially successful in the highly competitive individual grants with 3 ERC consolidators, 6 KWF young investigators, 5 VENIs, 2 VIDIs, 2 VICIs and 2 Amsterdam UMC fellowships (table VIII). Together worth around 18 million in competitive funds. Last but not least, the highly prestigious SPINOZA prize was awarded within this program.

Program 2: This program is the smallest in size with around 200 staff and around 160 PhD candidates. In terms of output around 1500 articles were published in the past 6 years of which 75-80% was OA. The program has made significant impact in specific areas and the metrics indicate a strong increase in output quality in the last years (table XIII). The imaging theme contributed strongly to the development of PET imaging and radiomics, specifically in lymphoma. A large international consortium was formed (www.petralymphoma.org) and artificial intelligence applied for better image analysis and patient stratification. Important steps were made in immunoPET, the development of novel radiotracers and application of existing tracers with total body PET-CT. In Biomarker development, significant impact was made in the analysis of platelets and vesicle from liquid biopsies for the detection of cancer. In addition, tools to identify stromal activation in the circulation were developed and used for clinical response evaluation, ultrashort DNA analysis developed as measure for tumor-derived cfDNA and proteomic analyses were designed on feces and bodily fluids to monitor disease. Enormous impact has been made in the program by screening efforts in colorectal, esophageal, head and neck, cervical and endometrial cancer of which some teams are studying the effect of nation-wide screening while others rather zoom in on optimizing screening on populations at risk.
Use cases (appendix 5,6,8 & 21) describe the successes of this program in a. designing the next generation imaging, and b. the use of liquid biopsies in disease monitoring. Besides the output, this program acquires around 11,5 million euro per year in competitive funding (table V). The variation from year-to-year is explained by the impressive success of this program in the acquisition of very large consortium grants. 2 large KWF consortium grants were acquired and 2 EU coordinatorships landed in this program (table VIII).

Program 3. This program has around 250 staff registered and the same amount of PhD candidates, but is by far the largest in terms of output, with close to 4000 publications over the years (table XIII). OA is improving strongly with 80% in 2021 and the average citation per paper is 13, but several publications have been cited more than 1000 times. The size of this program is also reflected in the input that is acquired. Of note, due to the strong translational emphasis of Cancer Center Amsterdam, part of the imbalance in output per program is due to a conscious registration bias, with especially immunology, biomarker and imaging studies being registered within this program even when they are published by PIs that are part of the other programs. That said, this program is evidently very strong with a large number of publications in leading medical journals (Lancet and JAMA journals, NEJM, 36 total in 2022 alone). The clinical domain made significant impact with several large clinical studies in hemato-oncology, pancreatic, esophageal and lung cancer, but also within screening for colorectal cancer.

In addition, enormous impact within QoL and supportive care research was evident. Specifically in the area of self-registration of QoL measures (Oncokompas), the influence of family involvement in cancer therapy or interventions on fatigue. In addition, the work on shared decision making and geriatric patients is noteworthy.
Use cases (appendix 18,22) that exemplify the success of this program describe a. the advances in pancreatic cancer therapy, b. implementation of shared decision making and Oncokompas and c. CAR-T cell developments.
This program attracts the largest amount of competitive funding, which is on average 15 million per year (table V). Also here variation is relatively large per year due to large consortia grants that have been acquired specifically in the last year. Success is also evident in individual grants with 3 young investigator grants from KWF and a VIDI, but has been specifically successful in the acquisition of consortia grants from KWF and the EU as well as in the acquisition of funds for multicenter trials (table VIII).

Business development achievements

Translational research in oncology knows many hurdles in ethical issues, legal matters, patient inclusion but also poses challenges in capacity and financing. To meet some of these challenges Cancer Center Amsterdam therefore professionalized its business development through the appointment of first 1 and later on 2 dedicated business developers. These are embedded in a larger tech transfer office but have a purely oncological signature and serve Cancer Center Amsterdam PIs only. Importantly, their role is to support our researchers in establishing connections to create economic or societal impact. That implies that Cancer Center Amsterdam made the strategic choice not to focus on possible facilitation of external partners, but to zoom in on reaching outward with our own research findings. Although the dedicated business developers were only appointed in the last part of the evaluation period their added value is already evident. In appendix 12, a total overview of the deal flow is presented, which includes 6 licenses of our IP, 12 public private partnership grants and a total of 132 research collaborations. Next to the support delivered by our business developers to individual PIs, the past 6 years has seen the initiation of or licensing to 3 start-up companies. The first example is CIMCURE that licensed the Booster vaccination technology developed by one our PIs. A similar technology licensing was agreed on with Qurin, which is based on the in house developed technology that enables the early detection of cancer in urine. Last but not least, LAVA therapeutics, was funded as a spin-off from Cancer Center Amsterdam developing bispecific gamma delta T cell engagers. In 2020 it received a 70 million euro investment and is currently listed at Nasdaq with bispecific antibodies in phase1/2a trials.

Future strategy

Cancer Center Amsterdam will finalize the process that it started in order to integrate its research and foresees to reach this milestone in 2025 when all activities are relocated to VUmc. Especially, the opening of the state-of-the-art research and diagnostic center (appendix 7) with integrated core facilities, GMP clean room, meeting facilities and intimately linked to the imaging center and hospital will strengthen our integration our preclinical and translational efforts. This milestone is however not the end of the integration as the next milestone will be to fully connect science with care. This phase has already been initiated in the past two years, but will require continued effort of the board of the cancer center as well as its research board. The external evaluation over the past 6 years is the ultimate moment to pass on the responsibilities for the coming years to a new director who will continue to foster research with the cancer center. Moreover, the research board will be complemented with additional theme leaders to secure that all themes will be spearheaded by both a preclinical and clinical theme leader.

The incentive to connect care and science will also entice the institute to extend its view to the outside world, both towards the region and beyond (inter)nationally. Importantly, the institute will not divert from its translational signature and will advance to bring biological and immunological insight towards the clinic and will continue to improve care through patient-centered research. It will make impact by taking a leading role in implementing novel therapies, in the innovation and implementation of supportive care but also in the early detection of cancer.

A SWOT analysis of the institute with the current strengths, weaknesses opportunities and threats is given in figure 10. Based on this our strategy going forward is defined.

	Helpful	Harmful
Internal factors	**STRENGTHS** • Vibrant community with (young) talent • Largest cancer center in the Netherlands • Patient-centered research focus • Internationally leading PI's • Strong position in clinical trials • Strong position in translational research	**WEAKNESSES** • Lack of dedicated research time clinicians • Split over many departments • Limited legal support • Lack of direct steering by institute and thus limited possibilities for strategic decisions • Limited possibilities for new staff positions
External factors	**OPPORTUNITIES** • Concentration to one site in near future • New high end facilities • Patient research groups • Regional/(inter)national collaborations • Interaction with neurosciences within ADORE • Valorization opportunities	**THREATS** • Increasing cost for personnel • Inflation for research equipment and reagents • Complexity funding • Complexity trial regulations • Increasing competition in recruitment of young talent • Relocation to VUmc will have impact on travel for part of the staff who may not join

Figure 10 SWOT analysis of the institute 2023

Specifically our strategy going forward addresses several key objectives.

Innovation through insight

The integration of research efforts of Cancer Center Amsterdam on one location assembles a powerhouse of pre-clinical and clinical research and forms a breeding ground for young talent and innovation. Our strategy will be to bring big data scientists, cancer biologist, immunologists, clinician scientists and patients together in one spot and expedite patient-centered research with excellent core facilities, but also with meeting places that allow for planned and spontaneous scientific interactions. We strongly feel that innovation cannot be forced but can be facilitated when talent is brought in the position to excel. As the location VUmc will house, next to the cancer center, the large Amsterdam Neurosciences (ANS) institute, a unique additional opportunity allows for an even more

innovation-oriented environment. ANS combines research and care of the brain and has several high profile research lines that include cell biology, drug screening, immune (dis)regulation and biomarkers, that easily align with those of Cancer Center Amsterdam. This has led to the bold plan to initiate the Amsterdam Oncology and Neurology research (ADORE) program (appendix 7). Connecting cell biology, immunology, drug or biomarker research in either discipline, will facilitate two important goals. 1. It will connect talented researchers and invite them to cross borders pushing innovation. 2. It will allow to build facilities that serve both disciplines, but more importantly attract leading specialist needed for such facilities. This strategy is currently already in place and working for the imaging facility where the total body PET-CT, acquired with private funds, not only serves the cancer community but is also essential for the brain research community. The shared experience acquired by the imaging specialists will propel this research area forward. In the coming years similar joined facilities will be built around Advanced Therapy Medicinal Products and iPSC products (GMP facility and iPSC unit), proteomics at single cell or organelle resolution. Liquid biopsies of cancer or neurology patients and CRISPR screening in complex model systems, such as organoids and iPSCs. All of these facilities will be incorporated in the new RDC building generating a nexus for innovation.
The focus of the cancer center will be to connect the biological insights obtained in cancer to personalized therapy and diagnostics.

Connecting science and care

The strategy to connect science with care is based on the vision that true translation will be expedited when all researchers have a clinical perspective and all caregivers have a research connection. To organize and consolidate our current translational aspirations, so called Patient-Research-Groups will be formed for the majority of patient groups we treat within Amsterdam UMC (appendix 24). The goal is to initiate PRGs for at least 80% of our patient groups and organize these along translational chains. This implies that PRGs are not only created around caregivers, but have an active involvement of preclinical researchers strengthening the interaction between pre-clinical and clinical research and driving bench-to-bedside-to-bench research lines. To further facilitate these translational efforts, Cancer Center Amsterdam will continue to support facilities that strengthen translation (LBC, Imaging) and connect these even better to the other two programs to explore new avenues of research such as the use of liquid biopsies in palliative care or the use of imaging to trace CAR-T cells. In addition, investments into new structures, such as Amsterdam Clinical Research Support (**ACRS**) will be made. The latter is crucial as clinical trial regulations are becoming a formidable challenge and the increasing complexity of trials calls for innovative trial design, while there is a growing awareness that enhanced data collection (omics) combined with optimized mining using artificial intelligence is needed. In the next years Cancer Center Amsterdam will within the ADORE initiative invest to address these challenges. Combined with the facilities that have been built, this strategy will help to consolidate our position in investigator-initiated trials, as partner for commercial collaborators, but also as leading institute in innovation of cancer care.

Connect with the region and beyond

Cancer Center Amsterdam has a proven track record in several impactful clinical trials. Such trials increasingly move towards patient-tailored therapies. While this is crucial to innovate cancer care, patient-specific clinical research inevitably requires low volume high complex clinical studies. To accommodate this, (inter)national collaboration is essential and our strategy is to take a leading role in international consortia and clinical studies. Importantly, this outward-looking collaborative attitude is also crucial for higher volume low complex studies and Cancer Center Amsterdam will invest in regional interactions as more and more patients are (in part) treated at regional hospitals. In line with this strategy is the alliance with our biggest partner, NKI-AvL, that has just been signed at the start of 2023 and which underscores and supports our vision to organize cancer care in the region. We have set a clear strategy to align care, but specifically also research in the region and will build a research network in the region that is called Run-for-the-region (appendix 23). This program is funded by sponsoring of the Amsterdam Marathon and KWF and will extend our research into the region, but is reciprocal in nature and will also allow regional experts to fully engage and contribute to our joined scientific goals. Run-for-the-region is closely aligned with our regional collaboration with all 13 hospitals in the region treating cancer patients. This OncoNoVo+ collaboration improves transmural cancer care, particularly for complicated patients or patients with rare cancers, but will also facilitate cancer research.

Detecting cancer early and personalized monitoring of treatment response

Early detection of cancer almost invariably improves therapeutic benefit for patients. Nevertheless, population screening is also a financial and potentially psychological burden on society. Non or minimal invasive strategies are key for the success of screening programs combined with a proper targeting of populations at risk. Similarly, detection of minimal residual disease to direct or refrain from additional therapy in individual patients, but also rapid detection of therapeutic benefit with highly sensitive, but minimal invasive, approaches will be crucial to monitor therapeutic benefit of often costly or burdensome therapies. Cancer Center Amsterdam will align novel biological insight with its efforts in imaging and biomarker development and its screening programs to improve on cancer detection. Moreover, the cancer center will focus on comprehensive stratification tools integrating imaging with molecular markers, to identify those patients who are likely to benefit and/or experience little side-effects from expensive novel drugs in order to make clinical and economic impact.

Reaching out to make impact

Cancer research and specifically patient-centered and translational research is becoming more complex to fund as it requires larger or more complex clinical studies, often expensive therapies or diagnostic tools. Cancer Center Amsterdam will therefore continue to bridge our science and innovation with commercial partners and will use its business development to implement this outward facing strategy. Accomplishing our goals will be expedited when these are co-developed by commercial partners. Similarly, we will make strategic decisions on the grant support that we offer. Consortia and collaborative efforts will be required to make the step towards translation and will therefore be prioritized.

Summary

Cancer Center Amsterdam was founded in 2016 by two scientific directors, a large team of PIs and an active staff of policy officers. With a strong emphasis on integration of all oncological research of AMC and VUmc, now merged into Amsterdam UMC, the institute embraced the goal to take an internationally leading position in translational oncology. Cancer Center Amsterdam is one of the eight research institutes within Amsterdam UMC with around 1200 active research members. However, it builds on a much larger team of professionals, as half way through the term that is under evaluation, Cancer Center Amsterdam made a strategic decision to connect care with science to facilitate its translational goals even further. This set the scene for a further integration of all oncological activities in Amsterdam UMC, the foundation of a daily board and the extension towards a more comprehensive cancer center. As a consequence, Cancer Center Amsterdam has become one of the largest cancer centers in Europe, integrating a multidisciplinary team of scientists that have expertise ranging from fundamental to clinical and QoL with care specialists and support staff.

Cancer Center Amsterdam's mission is to provide the best possible care for our patients today and tomorrow. We aim to innovate care through excellent patient-centered research and to improve therapy through biological insight into cancer and the generation of diagnostic tools and therapeutic modalities. Cancer Center Amsterdam's research is divided over three main research programs, Cancer Biology & Immunology, Imaging & Biomarkers and Clinical Therapy & Quality of Live. Programs are further sub-divided into 7 themes, each covering a specific domain within our research portfolio, and headed by theme leaders that oversee the activities within their area.

At the start the cancer center made a strategic decision to focus on translational science, to integrate scientific efforts and to invest in teams and facilities in order to supports its researchers. A multitude of events to integrate our science were organized, peer-to-peer support established and new facilities, equipment and joint projects were funded, while at the same time providing a platform to educate the next generation of researchers.

In the period under evaluation (2017-22) Cancer Center Amsterdam's researchers acquired more than 240 million euro in funding, which has led to ground-breaking research with more than 6000 peer-reviewed papers published. These are not only cited very well by colleagues in the field, hence fueling new research, but more importantly have made clinical impact. For instance, the institute was leading in improving therapy for several disease entities, including hemato-oncological and Gastrointestinal malignancies, but was also instrumental in the implementation of supportive care for patients with cancer. The success is further exemplified by the world-leading position that Cancer Center Amsterdam takes in the use of its publications in medical policy documents.

In addition, the impact made is seen by the >500 PhD candidates that have finalized their research and successful defended their theses. Trained within our graduate program, this young generation of scientists will continue their careers as medical specialists, pre-clinical researchers or continue in affiliated professions and are true ambassadors of our translational oncology research.

With 6 successful years behind us, we look forward to the coming period in which Cancer Center Amsterdam will finalize its integration at one location and is ready to take on the next challenge in further integrating oncological care with research. Valorization of our research will remain a cornerstone of our translational strategy, bringing research from the bench to the bedside and beyond to society. We look forward to an active role of the cancer center in the region and will continue to take up leadership in (inter) national clinical studies, societies and boards, all to make a positive impact on therapy and QoL of patients with cancer.

We are confident that the strong network organization that was built in the last years will continue to flourish, will remain a breeding ground for young talent and facilitate excellent translational research. Extending that effort beyond the walls of Cancer Center Amsterdam and to consolidate the alliance with our regional partners will open the door to further improvements in oncological care.

List of abbreviations

ADORE	Amsterdam Oncology and Neuroscience Research
AMC	Academic Medical Center Amsterdam
AML	Acute Myeloid Leukemia
ANS	Amsterdam Neurosciences
ARB	Amsterdam Research Board
ARCS	Amsterdam Clinical Research Support
ATMP	Advanced Therapy Medicinal Products
CAR-T	Chimeric Antigen Receptor-T cell
CB&I	Cancer Biology & Immunology
CCA	Cancer Center Amsterdam
CCA-APP	CCA - Ambulatory Patient outcome assessment Platform
CEC	CRISPR Expertise Center
CLL	Chronic Lymphocytic Leukemia
cfDNA	Cell-free DNA
CRC	Colorectal Cancer
CRISPR	Clustered Regularly Interspaced Short Palindromic Repeats
CWTS	Centre for Science and Technology Studies
EMA	European Medicines Agency
ErasmusMC	Erasmus Medical Center
ERC	European Research Council
EU	European Union
FAIR	Findable, Accessible, Interoperable and Reusable
FDA	U.S. Food and Drug Administration
FACS	Fluorescence-activated Cell Sorter
Ga	Gallium
GI	Gastrointestinal
GMP	Good Manufacturing Practice
HPB	Hepato-Pancreato-Biliary
JAMA	Journal of the American Medical Association
IB	Imaging & Biomarkers
iPSC	Induced Pluripotent Stem Cells
ITC	Immunotherapy Center
IXA	Innovation Exchange Amsterdam
KNAW	Royal Netherlands Academy of Arts and Sciences
KWF	Dutch Cancer Society
LBC	Liquid Biopsy Center
LiCl	Lithium Chloride
MNCS	Mean Normalized Citation Score
MRI	Magnetic Resonance Imaging
NEJM	New England Journal of Medicine
NKI-AvL	Netherlands Cancer Institute
NWO	Dutch Research Council
OA	Open Access
OOA	Oncology Graduate School Amsterdam
PDAC	Pancreatic Ductal Adenocarcinoma
PET-CT	Positron Emission Tomography - Computed Tomography
PI	Principle Investigator
PoC	Proof of Concept
PPS	Public Private Partnerships
R&D	Research & Development
QoL	Quality of Life
Rb	Retinoblastoma
RDC	Research and Diagnostic Center
SWOT	Strengths, Weaknesses, Opportunities and Threats
TKI	Top Consortia for Knowledge Innovation
TME	Tumor Microenvironment
TQL	Therapy & Quality of Life
UBVU	University Library Vrije Universiteit Amsterdam
UMCU	University Medical Center Utrecht
UvA	University of Amsterdam
VU	Vrije Universiteit Amsterdam
VUmc	Vrije Universiteit Amsterdam Medical Center
WHO	World Health Organization
ZonMW	The Netherlands Organisation for Health Research and Development

Tables

Table I List of Research board portfolios

Research Board portfolios
Grant support
Communication
Core facilities
Annual conference
Awards
Seminars and PI meetings
Talent program
Education
Business development
Patient-Research groups
IT, bioinformatics

Table II Cancer Center Amsterdam Equipment Investments

Projectnumber	Equipment	kEuros
CCA2018-5-42	Vectra Polaris Multispectral Imaging System	183
CCA2018-5-53	CCA Histology Imaging Facility	177
CCA2020-2-24	Da Vinci Surgical Robot	600
CCA2021-9-79	FACS Melody Cell Sorter	250
CCA2021-9-80	Incucyte Live-Cell Imaging System	150
Total		**1360**

Table III Stichting CCA projects

Projectnumber	Project title	Projectleader
CCA2016-1-20	eNose/IBD	
CCA2016-2-13	Antibodies pay Toll to improve their tumoricidal efficacy. - Targeted stimulation of immune responses at the tumor site-	Bakema, J.
CCA2016-2-14	Chemobrain	
CCA2016-4-08	ctDNA (liquid biopsies) as a marker for patients with peritoneal metastases of colorectal cancer, a clinical feasibility study	Tuynman, JB
CCA2016-5-27	Crossfire	
CCA2016-5-28	High Dimensional Mass Cytometry in Myelodysplastic Syndromes	Westers, TM
CCA2016-5-29	How tumors rewire metabolism and cell surface glycosylation patterns to remain under the immunological radar	Van Vliet, S
CCA2016-5-30	Guiding personalized therapy of patients with metastatic prostate cancer using a novel PET tracer: validation of 18F-radiolabeled PSMA	Oprea-Lager, D
CCA2016-5-31	Biological control of T-ALL	Illarregui, JM
CCA2016-5-32	The microbiome of pancreatic cancer: a correlation between bacteria and pancreatic cancer?	Giovannetti, E
CCA2016-5-33	Implementation of novel CRISPR/Cas9 technologies to reveal the functional significance of cancer associated genomic alterations	Van de Vrugt, H
CCA2016-5-34	IGFBP7 activates the retinoic acid differentiation pathway in acute myeloid leukemia (stem) cells; a therapeutic option to prevent relapse	Smit, L
CCA2016-5-35	Exosome-mediated delivery of miRNAs as anti-cancer therapy	Pegtel, M
CCA2016-5-36	Applying CIP to fast MR imaging	Cover, K
CCA2017-1-21	SUNRISE	

CCA2017-1-22	Plasma vesicle microRNAs for non-invasive therapy response evaluation, early detection of recurrence and treatment outcome prediction in patients with head and neck cancer	
CCA2017-1-23	FES-PET: towards a new standard to stage locally advanced and recurrent, estrogen receptor positive (ER+) breast cancer?	
CCA2017-2-15	Retinoblastoma	Moll, A
CCA2017-2-16	Cancer epi-transcriptomics: Differential RNA methylation as a molecular indicator of tumor progression in patients with diffuse low-grade glioma	Koppers-Lalic, D
CCA2017-4-09	Microbioom in pancreas carcinoom	
CCA2017-4-10	HM-DNA HLK	
CCA2017-5-37	HM-DNA	
CCA2017-5-38	Profiling of bone marrow microenvironment to improve diagnosis of myelodysplastic syndromes' bone marrow failure subtypes	Koning, J
CCA2017-5-39	Development of next generation hybrid therapeutic antibodies for B cell malignancies that enable short-term eradication as well as the induction of protective long-term adaptive immune responses	Heemskerk, N
CCA2017-5-40	Platform development for Artificial Intelligence-guided Radiomics and Image-based therapy in Head and Neck Cancer	de Graaf, P
CCA2017-5-41	CRISPR-Cas9 Based Functional Screening of Engineered Cell Models to Discover Genes that Drive Tumorigenesis and Determine Drug Responses	Wolthuis, R
CCA2018-1-24	the OPPERT study	Weijs, P
CCA2018-1-25	Supervised exercise to PRomote Infiltration of NK-cells into the Tumor? (SPRINT-pilot trial)	Buffart, L
CCA2018-1-26	Tumor concentrations and the effect of protein kinase inhibitors on phosphoproteomic profiles in patients with glioblastoma multiforme: an interventional, molecular profiling pilot study	Labots, M
CCA2018-2-17	PICTURE-project	
CCA2018-2-18	ADP Bloedplaatjes	
CCA2018-2-19	Glioma Drug Selection based on Poly-pharmacology, Access, Response and Kinetics (GlioSPARK study)	Westerman, B
CCA2018-2-20	GOALS: Glioma Oscillatory Activity as a potentiaLly Sensitive biomarker for tumor growth	Douw, L
CCA2018-4-11	Big Data Strategie	
CCA2018-4-12	Biomarker P-DAC	Van Vliet, S
CCA2018-4-13	ESMA-PET/CT imaging in the early detection of Cancer of the Prostate with High Risk Features (PEACH trial, a pilot)	Vis, A
CCA2018-4-14	Assessment of exocrine pancreatic insufficiency in patients who underwent resection for esophageal or gastric cancer	Straatman, J
CCA2018-5-43	Supraspliceosome	Koning, J
CCA2018-5-44	Irreversible electroporation and intratumoral administration of CpG as a means of in vivo vaccination for advanced pancreatic cancer	Scheffer, H
CCA2018-5-45	Assessing early treatment response to Radium-223-chloride and Rhenium-188-HEDP using 18F-Prostate Specific Membrane Antigen PET/CT	Oprea-Lager, D
CCA2018-5-46	MR-guided daily-Adapted organ-Sparing radiation Therapy for Early Recta! cancer (MASTER study)	Bruynzeel, A
CCA2018-5-47	Rational design of exosome-mediated CRISPR-Cas9 delivery for cancer gene therapy	Baglio, R
CCA2018-5-48	A mechanopharmacology approach to overcome chemoresistance in pancreatic cancer	Giovannetti, E
CCA2018-5-49	2-hydroxyglutarate; a metabolite that suppresses antitumor macrophage responses?	Van den Bossche, J
CCA2018-5-50	Atypic B cells in glioblastoma, a potential new target	Garcia Vallejo, J

CCA2018-5-51	Exploring the Lysosomal Stress Response, a New Cancer Driver, in 3D Cancer Models	Wolthuis, R
CCA2018-5-52	mTORture: Therapy for Replication-Stressed Cancers	Pai, G
CCA2019-1-28	Paulien study	
CCA2019-2-21	GRIP study	
CCA2019-2-22	18F-Prostate Specific Membrane Antigen PET-CT as a potential novel imaging modality for pancreatic cancer: A feasibility study (PANSCAN-2)	Swijnenburg, R
CCA2019-4-15	CAESAR study	
CCA2019-5-55	Nanocarriers for brain tumor therapy	
CCA2019-5-56	PANFIRE III	
CCA2019-9-57	Interfering with antigen presenting stromal cells in lymph nodes to block regulatory T cell conversion and boost antitumor immunity	Mebius, R
CCA2019-9-58	PD-L1 on the move; detecting extracellular vesicle bound PD-L1 for patient stratification	Crudden, C
CCA2019-9-59	Genome-wide identification of microRNAs involved in hyperthermia-induced radiosensitivity for optimized treatment of cervical cancer	Snoek, B
CCA2019-9-60	CATALASEing Fanconi Anemia: Mitochondrial Dysfunction as a Vulnerability in Fanconi Anemia Head and Neck Cancer	Zaini, M
CCA2019-9-61	Exploring and Exploiting Heat Shock to Sensitize Solid Tumors to Proteasome Inhibitors	Vriend, L
CCA2019-9-62	A computational framework to address within-tumour heterogeneity of pancreatic ductal adenocarcinoma	Kim, Y
CCA2019-9-63	Secreted vesicles, a signature of mesenchymal colorectal cancers?	Huels, D
CCA2019-9-64	Reprogramming the metabolic state of induced pluripotent stem cell (iPSC)-derived chimeric antigen receptor-engineered T cells (CAR T)	Themeli, M
CCA2019-9-65	Trafinibs: a targeted therapy to temper CAR T-cell associated toxicities	Seijkens, T
CCA2019-9-66	Immunotherapy and bloodvessel therapy	van Egmond, M
CCA2020-1-29	Aerobic fitness or Muscle mass training to Improve Colorectal cancer Outcomes (AMICO) - pilot trial	Versteeg, K
CCA2020-1-30	Whole-genome sequencing in patients with locally advanced (pancreatic) and metastatic solid tumors to identify molecular targets for (neo-)adjuvant and palliative systemic treatment	Labots, M
CCA2020-1-31	Exploring the dynamic relationship between the tumor microenvironment and the response to radiotherapy in esophageal adenocarcinoma	Derks, S
CCA2020-1-32	Diffuse B Cell lymphoma	Chamuleau, M
CCA2020-1-33	Immune-modulating effects of various doses of (chemo)radiotherapy and immunotherapy on tumor draining lymph nodes in stage II-III NSCLC	Fransen, Marieke
CCA2020-1-34	Mapping the human peritoneal immune system to identify novel immunomodulatory targets for the treatment of peritoneal metastasized cancers	Grootjans, J
CCA2020-1-35	Targeting and imaging glutamine metabolism in Chronic Lymphocytic Leukemia	Zijlstra, J
CCA2020-2-23	Integrated DataIntegrating multi-dimensional diagnostic data in cancer research: the next step in biology driven medicine using advanced analytics CCA-AvL-Hartwig	Kazemier, G
CCA2020-2-25	Towards optimizing and personalizing prehabilitation and multidisciplinary team meetings	Stam, W
CCA2020-2-26	A Phase I/II Proof-of-Concept Study of Somatostatin Receptor Type-2 Targeted Fluorescence Guided Surgery of Gastroenteropancreatic	Engelsman, AF
CCA2020-4-07	Pediatric acute leukemia	Kaspers, GJ
CCA2020-5-22	Machine learning glioblastoma	
CCA2020-5-23	OPRAH-pro study: Self-monitoring and advice on protein intake, integrated into an accelerometer-based physical activity intervention, to improve functional recovery in patients with cancer undergoing gastrointestinal or lung surgery.	Leeden van der, M

CCA2020-7-01	Respiratory mOtion-compensaTed Abdominal Tumour Imaging at high-resolutiON (ROTATION): Quantitative biomarkers and anatomical imaging	Gurney-Champion, O
CCA2020-7-02	Dynamic [18F]FES PET imaging in patients with metastatic ER+ breast cancer	Oprea-Lager, D
CCA2020-9-68	Computational approaches for predicting outcome parameters in myeloid neoplasms from clinical flow cytometry stem cell data	Bachas, C
CCA2020-9-69	Liquid biopsy-based immune profiling for cancer patients' personalized medicine	Baglio, R
CCA2020-9-70	Chromosomal instability as key regulator of the immune microenvironment of cancers	Miedema, D
CCA2020-9-71	In depth characterization of leukemia minimal residual disease using single cell transcriptomic analysis combined with quantitative cell surface protein profiling	Sie, D
CCA2020-9-72	Ovarian cancer detection by (epi)genetic biomarker analysis in urine	Steenbergen, R
CCA2020-9-73	Development of an in vitro human B-cell lymphoma model to study cancer dissemination	Winde de, L
CCA2021-1-37	Legaat Endel – Novel immunotargeting strategies in G-E Ca	Derks, S
CCA2021-1-38	The role of serum response factor (SRF) as a driver of chemoresistance in colorectal cancer	Lionarons, D
CCA2021-2-28	Optimizing lymph node staging in esophageal cancer with USPIO-enhanced MRI	Gisbertz, S
CCA2021-2-29	FAPI-PET for HPB cancers	Swijnenburg, RJ
CCA2021-5-24	PICTURE-4 project	
CCA2021-5-25	The GARP/TGF-β axis: a critical immune regulatory pathway in head and neck cancer?	Ven van de, R
CCA2021-5-26	Precision targeting of aminoacyl-tRNA-synthetases in cancer	Gerber, A
CCA2021-5-27	Multimodal image-guided resection of glioblastoma	Verburg, N
CCA2021-7-03	Artificial intelligence-based response prediction on diagnostic PSMA PET-CT as a tool for a personalized treatment approach in patients with metastatic hormone-sensitive prostate cancer	Oprea-Lager, D
CCA2021-9-74	Diffuse B Cell lymphoma	
CCA2021-9-75	Peritoneal metastases	
CCA2021-9-76	Genome-wide CRISPR screen for novel modulators of cancer exosome release	Crudden, C
CCA2021-9-77	Accurate isomiR detection for non-invasive PDAC diagnostics	Gómez, C
CCA2021-9-78	Identifying stromal regulators with therapeutic potential in pancreatic cancer	Gomes Leite de
CCA2022-1-39	Using bile cell-free DNA to discriminate between benign and malignant biliary strictures (BAMBI)	Voermans, R
CCA2022-2-31	OMEGA trial	
CCA2022-2-32	Reducing surgical overtreatment in patients with pT2 rectal cancer: expansion of criteria for rectum preserving, local excision as safe oncological treatment.	Wiggers, J
CCA2022-5-29	Database reserach glioblastoma	
CCA2022-7-04	B BB-ASL for injection-free G lioma B lood- B rain B arrier assessment: BIG-BBB	Mutsaerts, HJ
CCA2022-7-05	Towards resolving inconclusive staging of estrogen receptor-positive breast cancer: comparative Total Body PET/CT study using [18F]FES and [18F]F-FAPI-074	Zwezerijne, B
CCA2022-9-81	Oral Fecal Microbiota Transplant (FMT) Capsules from Healthy Donors in Patients with Locally Advanced, Resectable Gastric or Gastro-esophageal Junction Adenocarcinoma	van den Ende, T

CCA2022-9-82	Finding cohesin regulators to push cancer cells towards an early mitotic grave	Molenaar, T
CCA2022-9-83	Activating lung-resident memory T cells by local vaccine delivery to eliminate lung cancer	Affandi, A
CCA2022-9-84	Mapping T-cell dysfunction in the lymph-node 'cradle' of chronic lymphocytic leukemia; a single-cell, multi-omics approach	Peters, F
CCA2022-9-85	Targeting RNA modulators to enhance the effect of CAR-T cell immunotherapy	Foskolou, I
CCA2022-9-87	AML MRD measurement	
CCA2022-9-88	HOVON 143	
CCA2022-9-89	MDS kernonderzoek	
CCA2022-9-90	Targeting RNA modulators to enhance the effect of CAR-T cell immunotherapy	Bernink, J

Table IV Investments of CCA into facilities and projects

Year	Equipment/Facility/Project	kEuros
2016	Liquid Biopsy Center	270
2016	CRISPR/Cas platform	295
2016	Clinical trial support	150
2016	Ambulatory Patient outcome assessment Platform	300
2017	IncuCyte Live-Cell Imaging System	124
2017	Covaris E220 Focused-ultrasonicator	55
2018	Leica SP8 Falcon for lifetime imaging	70
2018	Nadia Single Cell Sequencer	50
2018	5 Nanodrop One Spectrophotometers	60
2019	UV laser for Cytek Aurora flow cytometer	60
2019	Gelcount colony counter	33
2019	qPCR Lightcycler	80
2019	Business Development	266
2020	Precision CellRad Cell Irradiation System	85
2020	Flow Conductor	80
2020	Liquid Biopsy Center	223
2020	Immunotherapy Center	300
2020	Gallium generator	288
2021	Hyperion imaging system upgrade	185
2021	R2 platform	320
2022	Nikon A1R confocal microscope	200
2022	Grant advisor	200
Total		**3694**

ADORE funds

Year	Equipment/Project	
2021	Total Body PET-CT scanner	5M
2022	PacBio sequencer	300k
2022	ADORE clinical research support	2,7M
Total		**8M**

Table V Acquisition of competitive funding total and per program

	Cancer Center Amsterdam					
	2017	2018	2019	2020	2021	2022
Funding type*	**M€**	**M€**	**M€**	**M€**	**M€**	**M€**
1st funds flow (estimate)	*31.4*	*28.8*	*27.8*	*29.6*	*27.9*	*29.6*
2nd funds flow	*4.5*	*4.8*	*5.9*	*4.7*	*6.8*	*6*
3rd funds flow	*25.8*	*20.6*	*19*	*18.5*	*18.1*	*23.3*
4th funds flow	*10.3*	*13.7*	*15.5*	*16.9*	*12.5*	*13.8*
Total funding	**40.6**	**39.1**	**40.4**	**40.1**	**37.4**	**43.1**
Total funding + 1st flow estimate	71	67.9	68.2	69.7	65.3	72.7

* 1st funds flow: direct funding estimated as 50% of staff salaries at average 150k total cost per core staff member
2nd funds flow: NWO, KNAW, government ministries, European organizations
3rd funds flow: Charitable organizations
4th funds flow: Research contracts with industry

	Cancer Center Amsterdam						
	2017	2018	2019	2020	2021	2022	Total
Funding type*	**M€**	**M€**	**M€**	**M€**	**M€**	**M€**	**M€**
2nd funds flow	*4.5*	*4.8*	*5.9*	*4.7*	*6.8*	*6*	*32.7*
Cancer Biol. & Imm.	*2.5*	*0.5*	*2*	*3.1*	*3.1*	*4.6*	*15.8*
Imaging & Biomarkers	*0.4*	*2.7*	*1.9*	*1.1*	*1.2*	*0*	*7.3*
Treatment & QoL	*1.6*	*1.6*	*2*	*0.5*	*2.5*	*1.4*	*9.6*
3rd funds flow	*25.8*	*20.6*	*19*	*18.5*	*18.1*	*23.3*	*125.3*
Cancer Biol. & Imm.	*10.4*	*10.6*	*6.8*	*8.6*	*8.3*	*5.1*	*49.8*
Imaging & Biomarkers	*8.5*	*5.7*	*8.1*	*4.6*	*3.8*	*3.8*	*34.5*
Treatment & QoL	*6.9*	*4.3*	*4.1*	*5.3*	*6*	*14.4*	*41*
4th funds flow	*10.3*	*13.7*	*15.5*	*16.9*	*12.5*	*13.8*	*82.7*
Cancer Biol. & Imm.	*1.2*	*2.6*	*2.3*	*0.9*	*2.8*	*2.2*	*12*
Imaging & Biomarkers	*0.8*	*6.7*	*6.3*	*9.3*	*3*	*3.7*	*29.8*
Treatment & QoL	*8.3*	*4.4*	*6.9*	*6.7*	*6.7*	*7.9*	*40.9*
Total funding	40.6	39.1	40.4	40.1	37.4	43.1	*240.7*
Cancer Biol. & Imm.	*14.1*	*13.7*	*11.1*	*12.6*	*14.2*	*11.9*	*77.6*
Imaging & Biomarkers	*9.7*	*15.1*	*16.3*	*15*	*8*	*7.5*	*71.6*
Treatment & QoL	*16.8*	*10.3*	*13*	*12.5*	*15.2*	*23.7*	*91.5*

Table VI Research output

	2017	2018	2019	2020	2021	2022	Total
Refereed	1048	1098	1127	1092	1276	1103	6744
Non-refereed	34	30	36	41	79	46	266
Other	32	23	28	27	49	11	170
PhD theses	82	69	74	95	99	87	506

Table VII Game changing studies

Tumortype	Study
Pancreas	PREOPANC-1
	LEOPARD-2
	ESPAC-4
	PRODIGE-24
CRC	CAIRO 3-6
Hemato-oncology	Daraturumab in multiple myeloma
	CAR-T in lymphoma
	MRD detection panel in AML
	Ibrutinib + Venetoclax in CLL (2x)
	Vaccination in AML
Brain cancer	cIMPACT-NOW
Esophageal	CROSS
Imaging	Guideline FDG PET/CT
	Brain PET guideline
QoL	Shared decision making
	Oncokompas

Table VIII highly competitive individual and consortium grants

Year	**Grant type**	**Acronym**	**Role**	**PI**
2017	ERC-Proof of Concept Grant	CTC4BMP	coordinator	Krishnadath, S
2018	Marie Curie-Innovative Training Network	COSMIC	coordinator	Guikema, J
2018	Marie Curie-Innovative Training Network	Elba	coordinator	Noske, D.
2018	ERC-Consolidator Grant	PRinTERs	coordinator	Wolkers, M
2019	H2020-Joint Techn Initiative Medicines	Immune-Image	coordinator	Windhorst, B
2019	ERC-Proof of Concept Grant	ERC - POCON	coordinator	Vermeulen, L
2019	ERC-Proof of Concept Grant	CHANCE	coordinator	Zelcer, N

2020	H2020-Joint Techn Initiative Medicines	RISCC	coordinator	Berkhof, H
2020	Marie Curie-Innovative Training Network	HYPERBOOST	coordinator	Crezee, J
2020	ERC-Consolidator Grant	Lab: BOOTCAMP	coordinator	Kater, A
2020	ERC-Proof of Concept Grant	NIMBUS4CIP	coordinator	Amant, F
2022	ERC-Consolidator Grant	ERC NIMICRY	coordinator	Vermeulen, L
2022	Marie Curie-Doctoral Networks	NADIS	coordinator	Houtkooper, R
2022	ERC-Proof of Concept Grant	Lab: CATCH	coordinator	Kater, A
2020	Marie Curie-Individual Fellowships	Michael Parkes	host	Bel, A.
2020	Marie Curie-Individual Fellowships	AngioCAR	host	Griffioen, A
2020	Marie Curie-Individual Fellowships	UNPACK PD-L1	host	Pegtel, M
2021	Marie Curie-Individual Fellowships	SENSOR - MSCA	host	Zelcer, N
2017	H2020-Joint Techn Initiative Medicines	ITCC-P4	beneficiary	Koster, J
2017	H2020-Joint Techn Initiative Medicines	HARMONY - IMI	beneficiary	Ossenkoppele, G
2017	Marie Curie-Innovative Training Network	META-CAN	beneficiary	Eldering, EF
2018	H2020-Future and Emerging Technologies	NICI	beneficiary	Laarhoven, H van
2019	H2020-Societal Challenges	LEGACy	beneficiary	Derks, S
2019	H2020-Societal Challenges	iPC	beneficiary	Koster, J
2019	Marie Curie-Innovative Training Network	PRECODE Marie Curie	beneficiary	Bijlsma, M
2020	European Regional Development Fund	Framome	beneficiary	Bijlsma, M
2020	European Regional Development Fund	Framome	beneficiary	Koster, J
2020	H2020-Joint Tech Initiative Medicines	Harmony Plus	beneficiary	Ossenkoppele, G
2020	H2020-Societal Challenges	H2020 Qualitop	beneficiary	Kersten, M
2020	H2020-Smart Cities and Communities	B1MG	beneficiary	Belien, J
2021	H2020-Joint Techn Initiative Medicines	H2020 T2EVOLVE	beneficiary	Kersten, M
2021	H2020-Joint Techn Initiative Medicines	H2020 T2EVOLVE	beneficiary	Themeli, M
2021	H2020-Societal Challenges	STOPSTORM	beneficiary	Balgobind, Br
2021	H2020-Societal Challenges	TIGER	beneficiary	de Gruijl, T
2021	H2020-Societal Challenges	H2020 RESILIENCE	beneficiary	Kersten, M
2021	HORIZON-INFRA-2021-Emergency funding	BY-Covid	beneficiary	Belien, J
2021	Marie Curie-Innovative Training Network	T-OP	beneficiary	de Gruijl, T
2021	Marie Curie-Innovative Training Network	EndoConnect	beneficiary	Zelcer, N
2021	Marie Curie-Res and Innov Staff Exchange	ALISE MSCA Rise	beneficiary	Giovannetti, E
2022	European Reference Network	GUIDELINES4RARE2	beneficiary	Eeghen, A van
2022	HORIZON-HEALTH	CANCERNA	beneficiary	de Gruijl, T
2022	HORIZON-HEALTH	CLASSICA (EU)	beneficiary	Tuynman, J
2022	HORIZON-HEALTH	GOLIAT	beneficiary	Vrijkotte, T

2022	HORIZON-HEALTH	EU NAVIGATE	beneficiary	VUmc
2022	HORIZON	CutCancer	beneficiary	van Maldegem, F
2022	Eurostars 3 call I	OpSIS	beneficiary	Griffioen, A
2017	KWF young investigator	Cohesion weakness	projectleader	de Lange, J
2018	KWF young investigator	prophylactic vaccination in MSI	projectleader	Bins, A
2018	KWF young investigator	Putting the patient at the center (of care)	projectleader	Braamse, A
2019	KWF young investigator	Head and neck cancer longterm survivorship	projectleader	Jansen, F
2019	KWF young investigator	Fertility preservation at cancer diagnosis	projectleader	Lehmann, V
2019	KWF young investigator	The growth of colon cancer	projectleader	Miedema, D
2020	KWF young investigator	antibody therapy and blood vessel inhibitors	projectleader	Heemskerk, N
2021	KWF young investigator	colon cancer is controlled by the ECM	projectleader	Huels, D
2021	KWF young investigator	peritoneal immunity	projectleader	Grootjans, J
2021	KWF young investigator	Development of MRI techniques to support personalized treatments for esophageal cancer	projectleader	Gurney-Champion, O
2017	KWF consortium grant	GLASS-NL	coordinator	Wesseling, P
2017	KWF consortium grant	ASAP-study	coordinator	Stoker, J
2017	KWF consortium grant	POWER	coordinator	Pieters, B
2018	KWF consortium grant	In search of stories: a narrative, multimodal spiritual care intervention for patients with incurable cancer	coordinator	van Laarhoven, H
2018	KWF consortium grant	Radiomics : Analysis of novel tumor features from PET/CT images of DLBCL patients for more effective therapy selection	coordinator	Zijlstra, J
2018	KWF consortium grant	Added value of liver MRI in patients scheduled for liver surgery due to metastatic	coordinator	Stoker, J
2019	KWF consortium grant	The phosphoproteome in CRC	coordinator	Jimenez, C
2017	NWO VENI	GastroeBoosting	projectleader	Derks, S
2019	NWO VENI	Mechanism of action of immunotherapy in HL	projectleader	Roemer, M
2020	NWO VENI	the role of regulatory T-cells in CRC	projectleader	Vieire Braga, F
2021	NWO VENI	Intercepting Cancer's Mail	projectleader	Crudden, C
2021	NWO VENI	Nanotrivax	projectleader	Affandi A
2018	NWO VIDI	BrainLayer	projectleader	Douw, L
2018	NWO VIDI	Sugary lipids impede proteins	projectleader	Spaapen, R
2019	NWO VIDI	Roles of tRNAs in Cancer	projectleader	Gerber, A
2022	NWO VIDI	Intercept	projectleader	van der Pol, E
2022	NWO VICI	Prevention is better than cure	projectleader	Vermeulen, L
2022	NWO VICI	Immunological memory in tissue	projectleader	van Gisbergen, K
2019	NWO Spinoza prize	Glyco-immunology	recipient	van Kooyk, Yvette
2017	New York Stem Cell Foundation award	Stem cells in CRC development and progression	recipient	Vermeulen, L
2021	Ammodo Science Award	Colon cancer research	recipient	Vermeulen, L

Table IX Panel, boards and editorships of CCA

Editorial boards of Journals	Grant panels	Board of societies
Nature Reviews Gastroenterology & Hepatology	European Haematology Association	Haemato Oncology Foundation for Adults (pres ex brd)
Gastroenterology	European Research Council (Chair)	American Radium Society (president)
Blood	French National Research Agency (ANR)	The Radiosurgery Society (president-elect)
Journal of Pancreatic Cancer (associate editor)	FWO (Research Foundation – Flanders) SBMED, Belgium (member)	European Society for Radiotherapy and Oncology (pres)
Acta Neuropathologica	KU Leuven Research Council	International Radiation Oncology Societies Network (pres)
Clinical Cancer Research	German Research Foundation Priority Programma “Radiomics” (member)	European Proteomics Association (vice-president)
Neuro-Oncology	German Research Foundation Priority Programme “Computational Connectomics” (member)	Netherlands Society of Gene and Cell Therapy (president)
Journal of Experimental & Clinical Cancer Research (associate editor)	Health Research Council of New Zealand	Dutch Cancer Society workgroup Psychosocial Oncology (chair)
Journal for Immunotherapy of Cancer	Institut National du Cancer, France (member)	Dutch Society for clinical radiochemistry (chair)
Cancer Immunology Research	AIRC (Italian Cancer Research Foundation)	European Hematology Association (chair)
Cell Death and Differentiation (assistant editor)	Austrian Science Fund	European Organization of Research and Treatment of Cancer – Pharmacology and Molecular Mechanisms (chr)
Journal of Nuclear Medicine	Cancer Research UK (member)	European Society for Medical Oncology upper GI faculty
Haematologica	Medical Research Council (UK)	Haemato Oncology Foundation for Adults Imaging working group (chair)
Angiogenesis (editor in chief)	Wellcome Trust (United Kingdom)	Haemato Oncology Foundation for Adults CLL working group (chair)
Angiogenesis (board)	Deutsche Forschungs Gemeinschaft	Haemato Oncology Foundation for Adults Echelons in Hematological Care (chair)
Endoscopy	Natural Science and Engineering Research Council of Canada	Haemato Oncology Foundation for Adults Lymphoma Working Group (chair)
Gastrointestinal Endoscopy	NeuroOncology Research Program Heidelberg Germany	Haemato Oncology Foundation for Adults Multiple Myeloma working group (chair)
European Journal of Nuclear Medicine and Molecular Imaging	Polish National Science Center (NCN panel)	International Burkitt Lymphoma Network (chair)
Blood Cancer Journal	Swedish Science Society	International Myeloma Society

Neuro-Oncology Advances	Swiss National Science Foundation	Preclinical Dutch Pancreatic Cancer Group (chair)
Frontiers in Immunology	Cure for Cancer Association (member)	Society for Cancer Biology of the Dutch Cancer Society (ch)
Frontiers in Immunology (associate editor)	International Waldenstrom Macorglobulinemia Foundation (IWMF), USA (member)	Cancer project of the Human Proteome Organisation (co-chair)
Blood Advances	The Netherlands Organisation for Health Research and Development	European Retinoblastoma Group (co-chair)
Brain Pathology	TKI-health Holland	Dutch Fluorescence-Guided Surgery Group (treasurer)
Molecular and Cellular Proteomics	KWF Dutch Cancer Society	European Organization for Research and Treatment of Cancer
Cellular Oncology (associate editor)	Dutch Foundation for studies of Gastrointestinal Diseases	Dutch society of Nuclear Medicine (board member)
Radiotherapy and Oncology	Dutch Research Council	Society of Radiopharmaceutical Sciences (board member)
Oncogenesis (associate editor)	Dutch Uro-Oncology Association (member)	Society for the Immunotherapy of Cancer (board member)
Oncogenesis (Editor)	Oncode	ACE incubators
Neuropathology Applied Neurobiology	Ministry of Health, Welfare and Sport	Amsterdam Young Academy Dutch Network Science Society
International Journal of Molecular Sciences	French Ministry of Health and the National Cancer Institute of France (member)	Association for Cancer Immunotherapy
Cancers	Society for Immunotherapy of Cancer	Cure for Cancer
Frontiers in Oncology	BRAINS programme for cross-disease neurological research (member)	Dutch Breast cancer group
Lung Cancer (section editor for radiotherapy)	Scientific Board at Fondazione IRCCS Istituto Nazionale dei Tumori, Milano	Dutch Clinical Physics Association
Frontiers in Pharmacology of Anti-Cancer Drugs	Joint Programma Neurodegenerative Disease Research	Dutch Hematology Association
Oral Oncology	King Baudouin Foundation, Fund Maaike Lars Trees, Belgium (member)	Dutch Hepatobiliary Audit (member)
The Oncologist (section editor for radiotherapy)	Weizmann Institute of Science	Dutch Pancreatic Cancer Group
Advances in Cancer Biology - Metastasis (section editor)	La Caixa, INPhINIT program (member)	Dutch Radiology Society
Clinical and Experimental Immunology	Lymph & Co	Dutch scientific association of Psycho-Oncology (member)
British Journal of Surgery	Melanoma Research Alliance	Dutch Society for Hematology
Frontiers of Medicinal and Pharmaceutical Chemistry	Anne Reynvaan grants	Dutch Society for Immunology
Therapeutic Advances in Medical Oncology	Nelly Reef Fund	Dutch Society for Radiotherapy and Oncology
Human Brain Mapping		Dutch Techcentre for Lifesciences

Journal of Molecular and Cellular Medicine	Dutch Thyroid Cancer Group
Clinical Proteomics	Dutch Upper-GI Cancer Group (member)
Scientific Reports	Dutch Urology Society
Human Gene Therapy	Dutch Uro-Oncology Association
Medical Physics	European Society for Gastrointestinal Endoscopy
World Journal of Clinical Oncology	European Society for Radiotherapy and Oncology
Journal of Neuro-Oncology	European Society of Medical Oncology
Biomedcentral Cancer	European Association of Nuclear Medicine
European Journal of Surgical Oncology	European Association of Urology
Journal of Proteomics	European School of Hematology
Journal of the Anus, Rectum and Colon	European Organization of Research and Treatment of Cancer – Pharmacology and Molecular Mechanisms
European Journal of Nuclear Medicine and Molecular Imaging - Research	European Research Initiative of CLL
Anticancer Therapeutics (section editor)	European Society of Digestive Oncology
Journal of Biomedical Optics	European Society of Oncologic Imaging
Proteomics	European Society of Urologic Radiology
Molecular Imaging and Biology	European Urology Robotic Urology Section
Cancer Chemotherapy and Pharmacology	European Workshops on Cell Death
Lasers in Medical Science	Fanconi anaemia Europe
Journal of Chemotherapy (associate editor)	Foundation for the National Institutes of Health Biomarkers Consortium
Cancer Drug Resistance	German Hodgkin Study Group Steering Committee
Brachytherapy journal	Haemato Oncology Foundation for Adults Lymphoma working group (member)
Canadian Respiratory Journal	Haemato Oncology Foundation for Adults Imaging working group (chair)
Journal of Labeled compounds and radiopharmaceuticals (editor)	Head and Neck Centre Liverpool
Journal Contemporary Brachytherapy	International Association of Cancer Registries
European Journal of Cancer Care	

International Journal of Cancer	International Conference on Physical Therapy in Oncology
Neuro-Oncology Practice	International Cytokine & Interferon Society
Current Cancer Therapy Reviews	Life Science Make Better foundation
Reports of Practical Oncology and Radiotherapy	Molecular Diagnostics Hematological Malignancies (board)
International Lung Cancer news (IASLC)	Netherlands Proteomics Platform
Dutch Nursing Journal: TVZ (editor in chief)	Netherlands Society for Extracellular Vesicles
Proteomics Clinical Applications	Onconet (founding board member)
World Journal of Pharmacology	Paediatric Radiation Oncology Society
Dutch Hematology Journal	Radiological Society of North America
Nederlands Tijdschrif voor Geneeskunde	RNA society
Urograaf (Dutch Urology Journal)	Society of Radiopharmaceutical Sciences (board member)
Clinical endoscopy	World Endoscopy Organisation
	ZonMW Veni (vice chair)
	DHCG, DGOG, DMSCG, DMTR groups

Table X Cancer Center Amsterdam staff

	Cancer Center Amsterdam					
	2017	**2018**	**2019**	**2020**	**2021**	**2022**
Scientific core staff	418	384	371	395	372	394
Assistant professor	*-**	*-*	*-*	*45*	*56*	*60*
Associate professor	*-*	*-*	*-*	*36*	*39*	*41*
Full professor	*-*	*-*	*-*	*148*	*146*	*144*
Other staff	*-*	*-*	*-*	*166*	*131*	*149*
Other scientific staff	178	176	149	179	172	245
Postdocs	*150*	*153*	*133*	*159*	*154*	*163*
Other researchers	*28*	*23*	*16*	*20*	*18*	*82*
PhD candidates	512	547	562	580	552	571
Visiting fellows	20	15	11	11	11	6
Total research staff	**1128**	**1122**	**1093**	**1165**	**1107**	**1216**

* Registration of Assistant, Associate, and Full professors per type was performed from 2020 onwards

Table XI Open Access publishing

	2017	2018	2019	2020	2021	2022	Total
N pubs	914	997	1063	1005	1192	933	6104
P (OA)	593	717	763	830	946	247	4096
PP (OA)	0.65	0.72	0.72	0.83	0.8	0.69	0.74

numbers of analyzed publications do not fully overlap with total output due to a difference between web of science (used for this analysis) and Pubmed listing (used for our registration)

Table XII Professor appointments at Cancer Center Amsterdam

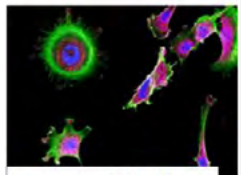
	total 2022	% female	Appointed 2017-2022	% female
Professor	144	28%	40	38%
Ass. professor	41	39%	18	39%
PIs	171	35%	46	43%

Table XIII Data staff and publication metrics per program

Input (2022)	CCA total	CBI*	IB*	TQL*
Scientific core staff	394	*170*	*129*	*172*
Assistant professor	*60*	*30*	*19*	*18*
Associate professor	*41*	*14*	*20*	*12*
Full professor	*144*	*76*	*54*	*67*
Other staff	*149*	*50*	*36*	*70*
Other scientific staff	245	*151*	*68*	*80*
Postdocs	*163*	*116*	*46*	*45*
Other researchers	*82*	*35*	*22*	*35*
PhD candidates	571	266	153	226
Visiting fellows	6	1	1	4
Output (2017-2022)	**CCA**	**CBI**	**IB**	**TQL**
Refereed	6744	1653	1451	4079
Non-refereed	266	63	15	92
Other output	170	25	24	133
Non-cited work	3.4%	1.9%	4.5%	5.3%
Average citations	15.1	16.6	15.1	13.8
MNCS 2017-2019	2.02	1.95	1.73	2.13
MNCS 2020-2022	2.20	1.66	2.41	2.32
# papers >1000 citations	6	1	2	3
# papers >200 citations	59	17	12	32
# papers >100 citations	128	36	26	72

*articles or staff can occur in 2 programs
CBI = Cancer Biology & Immunology
IB - Imaging & Biomarkers
TQL - Treatment & Quality of Life

Appendix 1: Programs of Cancer Center Amsterdam



Cancer Biology

Eric Eldering | Renske Steenbergen | Louis Vermeulen | Rob Wolthuis

Cancer Immunology

Marjolein van Egmond | Arnon Kater | Tanja de Gruijl | Rosalie Luiten

Target & Therapy Discovery

Marcel Spaargaren | Victor van Beusechem | Sheila Krishnadath | Ruud Brakenhoff

Imaging

Hanneke van Laarhoven | Ton van Leeuwen | Josee Zijlstra | Guus vDongen

Biomarkers

Maarten Bijlsma | Michiel Pegtel | Evelien Dekker | Connie Jimenez

Therapy

Supportive care

Suresh Senan | Arjen vd Loosdrecht | Marc v Berge Henegouwen | Lukas Stalpers

Heinz-Josef Klumpen | Martijn van Oijen | Donald vd Peet | Laurien Buffart

Irma Verdonck | Jaap Rijneveld | Martha Grootenhuis | Mirjam Sprangers

SELF-EVALUATION

Oncologie Onderzoekschool Amsterdam

- OOA -

Oncology Graduate School Amsterdam

Introduction

The training of Cancer Center Amsterdam's PhD candidates is embedded in the Oncology Graduate School Amsterdam (Onderzoekschool Oncologie Amsterdam – OOA). The OOA is a large and successful school, home to over 1,000 PhD candidates of many nationalities employed at two state-of-the-art institutes, Amsterdam UMC and NKI-AVL. Our mission is to provide a broad range of high-quality theoretical and practical courses in oncology, and to ensure proper supervision of PhD candidates. The fruitful collaboration between the two institutes provides PhD candidates the opportunity to learn from and collaborate with many internationally recognized scientists. Please watch our video for an impression of our school.

OOA TEAM

Deans

Prof. dr. Arjan Griffioen, chair
Prof. dr. Hein te Riele
Dr. Marcel Spaargaren

Coordinator

Dr. Esther M. Ruhé

Support Staff

Evelien Bos, Noëlle Commandeur, Theo Lamers

PhD candidate council

Barbara Andrade Barbosa, Ben Ooms, Chavelli Kensen, Konstantina Strepi, Maud Schoot Uiterkamp, Britt van der Swaan, Maxime

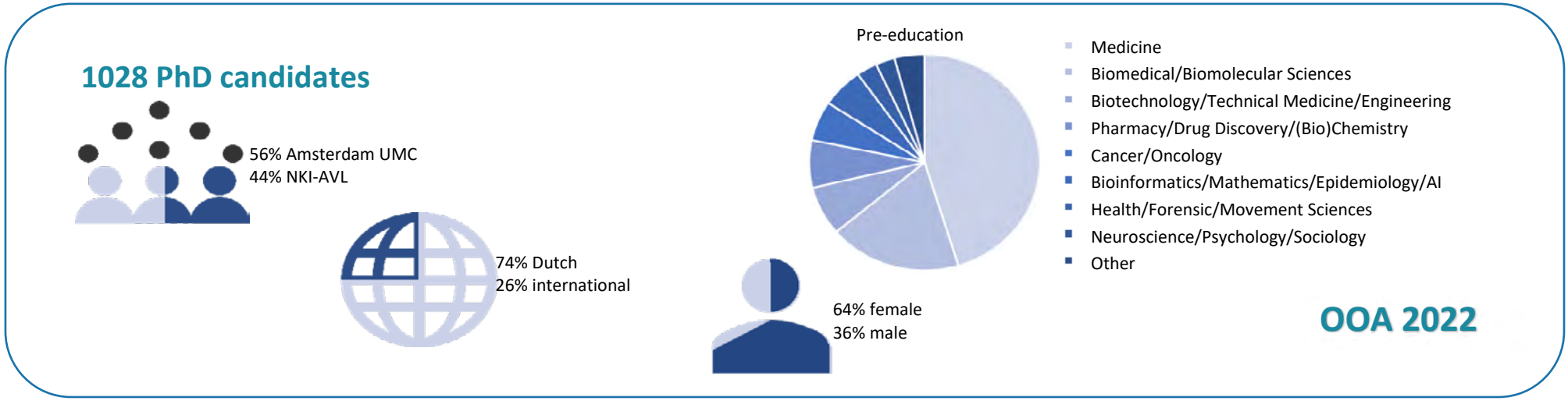
Organizational information

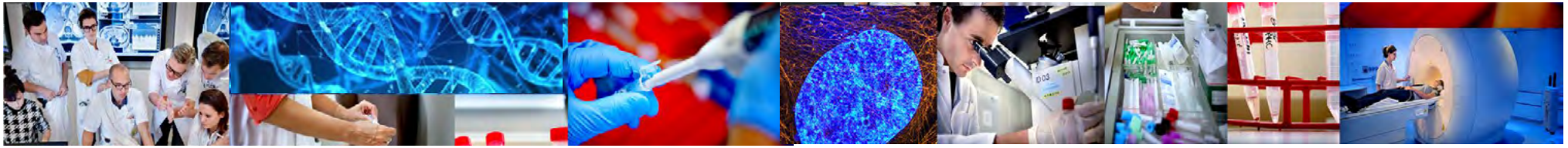
The OOA is managed by an executive team of three deans, all acknowledged scientific cancer researchers at Amsterdam UMC Cancer Center Amsterdam (CCA) and NKI-AVL, and a coordinator. The executive team is responsible for the education program, and the design and implementation of OOA policies. They are assisted by a support staff. The central administration is located at Amsterdam UMC – location VUmc.

The interests of PhD candidates are represented by a PhD candidate council. The council advises the executive team on the course program and organizes (social) events to stimulate close connections between PhD candidates. It is made up of PhD candidates from each institute with different nationalities, and serves as a bridge between individual Dutch or international PhD candidates and the management team.

The education program is financed by Amsterdam UMC and NKI-AVL, according to the ratio of participants from each institute. Thanks to these contributions, the OOA PhD candidates can participate in all educational activities free of charge. For an overview of our finances 2017 – 2022 please click here.

> **"The OOA is the glue for all oncology PhD candidates in Amsterdam and allows for meaningful scientific and social interactions through the provision of courses and events related to science and personal development."** Chavelli Kensen, OOA PhD councilmember





Training and education

To prepare PhD candidates for a successful career inside or outside academia, we aim to provide them all the same solid foundation. To this end, we implemented a uniform and mandatory training and supervision plan (TSP) in 2021. This plan was based on the best practices of the regulations that were in place at our affiliated institutes. It contains a number of mandatory activities, supplemented by education and activities that can be tailored to each candidate's own interest, backgroud and needs.

At the start of their PhD training, all PhD candidates must make an initial plan in consultation with their supervisor. During the course of the PhD trajectory, the TSP can be adjusted where necessary. We monitor this process and provide advice if needed. At the end of the PhD program, we review the TSP and award an educational certificate when all criteria are met. This procedure, which is described on our website, is brought to the attention of all starting PhD candidates as soon as they are registered at the OOA. To guide and inform them even more (inter)actively, we are currently working on a onboarding starters package.

Training requirements

30 ECTS total (1 ECTS = 28 hours)

Mandatory 2 ECTS 'Ethics and Integrity in Science' course

≥ 8 ECTS professional knowledge and general skills courses

≥ 1 scientific conference

Additional courses and activities, writing articles, teaching, retreats, group meetings, etc.

Course program

We have a longstanding tradition of offering courses, workshops and educational events. We are very proud that we have managed to maintain our course program during the COVID-19 pandemic by converting our courses to online editions, thanks to the flexibility of the course organizers, teachers, as well as the PhD candidates. Click here for an overview of our course program 2017-2022.

Over the last four years, we have doubled our activities. We have to further expand our offerings to provide the growing number of PhD candidates (800 in 2017 to 1000 in 2022) adequate opportunities to meet the mandatory training requirements. Additional budget, to be provided by Amsterdam UMC and NKI-AVL, are necessary to meet this demand.

Our PhD candidates work in a wide range of oncology-related projects, from experimental biology exploring oncogenesis and tumor cell biology to clinical research addressing prevention, diagnosis, treatment and quality of life. To provide a solid foundation in the many aspects of oncology, we offer the Basic Oncology course. Once familiar with the basic principles, they can subsequently choose courses focusing on more specific scientific topics such as tumor types or new groundbreaking technologies. The course program is dynamic: new advances in cancer research and care, educational needs and evaluations of former courses all influence the course content. The OOA PhD council recently conducted a survey among all PhD candidates, enabling us to address the specific needs expressed by the individual PhD candidates. Candidates make a selection according to their interest and background. We announce our courses on our website and send email notifications.

We highly value the translation of basic research findings into clinical applications, and vice versa. To promote this, our three-day annual retreat - entirely focusing on the research conducted by the candidates - is a unique event that fosters collaboration and expands our candidates' awareness of cutting-edge oncology research outside their immediate environment.

To further stimulate cooperation and exchange of knowledge and techniques between NKI-AVL and both locations of Amsterdam UMC, we are planning a scientific online networking platform that spans both institutes. Furthermore, we will organize tours to the state-of-the art facilities that are available at both institutes, aiming to create awareness and motivate the candidates to consider utilizing these facilities for their own research.

Courses are typically organized by the OOA executive team and/or a team of principal investigators (PIs) invited by the executive team. Because more than 200 oncology PIs are affiliated with Amsterdam UMC or NKI-AVL, we have the opportunity to offer a very broad range of course topics. Quality assurance is carried out by applying the

PDCA cycle (Plan, Do, Check, Act). All courses are evaluated by the participating candidates. Course organizers discuss these evaluations with the OOA executive team and take action accordingly. Amsterdam UMC offers several training programs for lecturers.

We closely collaborate with the Amsterdam UMC Doctoral School, which provides training in general/soft skills. Thanks to the co-existence of the OOA and the Doctoral School, Amsterdam UMC PhD candidates have the unique opportunity to follow a supplementary educational program that is focused on both professional and personal development. Previously, the Doctoral School courses were only available to Amsterdam UMC PhD candidates. We are currently conducting an inventory with the Doctoral School to determine if the courses can also be made accessible to all NKI-AVL candidates. In addition to the local educational activities, PhD candidates are also encouraged to apply for externally organized courses, including those organized by our partner schools Medical Genetics Centre South-West Netherlands and the Utrecht Clinical and Translational PhD program. PhD candidates from these schools are also invited to attend OOA courses.

4.2 average evaluation rate of our courses (1 – 5 point scale)

3901 course participants

1.4 ECTS average number of credits per

79 course organizers

122 educational activities

"The OOA is irreplaceable, as it provides over a thousand PhD candidates with courses and workshops, that span the broadness of the oncology field."

Ben Ooms, OOA PhD councilmember

Supervision, monitoring, counseling and well-being

It is essential that PhD candidates receive thorough and intensive guidance throughout their PhD. Several levels of support and supervision are in place:

1. **Personal guidance by the promotor.**
The promotor, often assisted by a daily supervisor, has the primary responsibility of giving all necessary feedback and support. At Amsterdam UMC and NKI-AVL, leadership, courses are offered for supervisors.

2. Mandatory training and supervision (TSP) plan.
The TSP assures that the research & training plan and evaluation meetings are well documented right from the start.

3. Monitoring progress by independent researchers.
This periodic review, ensures independent oversight and advice.

4. Independent local confidants/counselors.
PhD candidates can seek assistance when experiencing conflicts or issues related to scientific integrity, undesirable behavior or discrimination.

5. Mandatory OOA Ethics and Integrity in Science course.
This provides an essential benchmark for integrity and ethical issues, as well as an overview of all available resources and counselors.

6. Mentorship program.
This successful program from Amsterdam UMC CCA/AII connects junior with senior researchers.

7. Psychological support.
Ranging from one-on-one professional psychological support to guided or non-guided peer intervision groups,

Some of these support systems are organized by the institute for all employees, including PhD candidates. We recently created a summarizing OOA webpage. All this information will also be part of our onboarding starters package.
We will monitor if the above-mentioned support is sufficient to ensure our candidates are well-equipped to overcome the challenges they may face. If not, actions will be taken accordingly.

Intake, duration PhD projects and career prospects

Analysis of the progress of 755 PhD candidates who started their PhD program between 2014 and 2018 showed that 10% and 21% PhD candidates completed their PhD program within 4 and 5 years, respectively (click here for details). The average duration from start to thesis completion for the 595 PhD candidates who defended their thesis in 2017 to 2022 was 5.7 years (69 months, see here), slightly higher than the national average of 61 months (VSNU). On the other hand, the average drop-out rate is lower than the Dutch average of 25% (Rathenau). It should be mentioned that the OOA has little influence on the duration of the PhD trajectory, e.g. many PhD contracts involve clinicians who combine their PhD research with clinical care. About 70% of the Amsterdam UMC PhD candidates who did not graduate within 7 years was enrolled in a medical residency during the PhD program.

The career prospects of our PhD candidates are excellent. Of the 518 OOA alumni analyzed, the majority secured positions that match their level of training, with many continuing their careers in medicine. This is in line with the high intake of PhD candidates with a medical background. The percentage of our graduates who find jobs in research at universities or other academic centers aligns with the national average (31% of all PhD candidates, Rathenau).

A number of PhD candidates will pursue careers outside of academia. That is why we strive to prepare our candidates for all career opportunities. Each year, we organize the BioBusiness course. In 2020, we offered a pilot "Holy Sh*t Show" that focused on matching career choices with needs and aspirations. In 2022, the NKI PhD council organized a successful local event where OOA alumni presented their career track, followed by an informal pizza meeting enabling the PhD candidates to connect with the alumni. Moving forward, we plan to implement the most successful pilots into annual recurring events to help prepare our candidates for their future careers.

alumni 2017-2022

- 14% commercial sector
- 51% residency/ medical doctor
- 27% researcher academic center/university
- 8% non-profit sector

Talent Policy and societal impact

In 2015, we initiated the NWO-funded OOA Diamond Program, which supported four exceptional master's students to design and conduct their own PhD research. The program was successfully completed this year. Allowing students to choose a research group and pursue their own research interests turned out to be highly motivating and led to impressive research output. We are very proud of the four Diamond PhD candidates for publishing their scientific accomplishments, initiating new international collaborations and receiving grants and prizes. Click here for more information about the Diamond Program and results. We have proven that the Diamond Program attracts and retains talented students and results in better integration of Master's and PhD programs. Financial support is necessary to secure continuation of the Diamond Program.

In 2021, we launched the pilot 'Masterclass' program with the goal of introducing cancer research to the next generation of students, cultivating their awareness and enthusiasm for this field. In collaboration with a Dutch pre-university secondary school (VWO), we organized Masterclasses for VWO students (read more). These Masterclasses, taught by enthusiastic OOA PhD candidates, proved to be a success. More than 200 pre-university students learned about cancer and cancer research in an accessible and interactive way. It also enabled OOA PhD candidates to share their knowledge while also learning to pitch their research. We received positive feedback from schools as well as students, with an evaluation score of 4 (scale 1-5). Encouraged by this success, we plan to further expand this program to more secondary schools in the Amsterdam region.

SWOT analysis

STRENGTHS

- Connects two prestigious institutes with an extensive community of teachers.
- Uniform, well-organized mandatory Training and Supervision Plan
- Wide range of educational activities and improved mental health support.
- Connects highly divergent fields of oncology.
- Close cooperation with the Amsterdam UMC Doctoral School.
- Good cooperation within OOA team and enthusiastic and proactive council.
- Large number of PhD candidates; continuity and networking opportunities.
- Location: the capital of the Netherlands, attracts speakers and PhD candidates.

WEAKNESSES

- The large number of enrolled PhD candidates are scattered at different locations, making it challenging to foster a closely connected community.
- Regulations are not immediately clear to all starting PhD candidate.
- Underrepresentation of translational and clinically-oriented courses.
- Not enough implemented educational activities about career opportunities.
- The OOA has no mandate to directly influence the duration of PhD trajectories.

OPPORTUNITIES

- All AMC CCA researchers, will move to location VUmc in the near future.
- Collaboration opportunities: letter of intent signed by A'dam UMC and NKI.
- Commitment of the Doctoral school to organize general/soft skills courses.
- Successful outreach to local pre-university schools to increase awareness of cancer research career opportunities.

THREATS

- No financial budget that can be independently spent.
- Discontinuation of the Diamond Program due to lack of financial resources.
- Expanding our course program to keep up with the increasing number of PhD students is challenging.
- Reduced motivation of students to take a look over the fence, due to increased pressure.

Future Plans

To further increase the impact of our school, we have – in consultation with the PhD council - formulated several goals that we will pursue the coming years. To meet the growing educational need of our PhD candidates, we have to expand our course offerings and capitalize more on collaborations with the Doctoral School and other Dutch graduate schools. We are planning to include more courses on translational & clinical research, new evolving research fields such as AI, and organize events to create more awareness about career opportunities.

To professionalize our communication strategy, we will **create a starters package** to smoothly engage all new PhD candidates and to introduce them to the full range of activities, services and support available. To foster collaboration, also between clinical and basic researchers, we will **create a networking platform** and organize research facility tours. The formation of a network/platform will be strengthened through the introduction of a renewed website and a newsletter. These improvements enhance communication channels and also serve as effective tools for recruiting and engaging prospective PhD candidates. To attract motivated and promising cancer researchers in the future, we will **extend the masterclasses** at pre-university schools and apply for funding at the participating institutes and/or external sources to revive and secure the **Diamond Program.**

Appendix 3: CRISPR expertise center

Boosting Cutting Edge Technology to Accelerate Discoveries

The CRISPR Expertise Center Cancer Center Amsterdam allows researchers to harnessing the power of the cutting edge CRISPR technology quickly in a collaborative environment.

Few today have not heard about CRISPR/Cas, the unique *technology* that enables geneticists and medical researchers to edit designated parts of the genome. Heralded as a true gamechanger in biomedical research, Cancer Center Amsterdam seized upon the opportunity to harness the power of CRISPR/Cas by establishing our CRISPR Expertise Center in 2018.

In 2020, Emmanuelle Charpentier and Jennifer Doudna received the ultimate science prize - the Nobel Prize in Chemistry - for discovering CRISPR/Cas9 genetic scissors. This recognition underscored the vast potential of this revolutionary gene editing technology in various fields, particularly medicine.

Since the adaptation of CRISPR from bacterial immune system into a workhorse for scientific discoveries, a vast tsunami of biomolecular assays and cancer research tools has been developed, offering exciting new opportunities to our researchers.

To expedite CRISPR applications and assist researchers in fully utilizing this unprecedented technology, the CRISPR Expertise Center (CEC) was established through a strategic investment by Cancer Center Amsterdam in 2018.

The CEC provides expert advice, training, and reagents, in addition to collaborative research options. The CEC has successfully introduced or accelerated the use of the CRISPR technology in many labs at Cancer Center Amsterdam - from creating gene knockouts, regulating gene expression, to facilitating genome-wide genetic screens and developing the next generation of CAR T-cell therapies.

The combined expertise and molecular resources available at the center have empowered research projects at Cancer Center Amsterdam to fully exploit the technical revolution CRISPR unleashed, taking research projects to a new level and catalyzing research output and success rates of grant applications.

CEC Manager

To enhance interactions and dissemination of knowledge, the CEC Manager Dr. Leite de Oliveira, Assistant Professor at the Dept. of Human Genetics, is stationed ‘50-50’ at both VUmc and AMC locations. Over the years, several R&D areas have been identified upon consultation with the CCA community, including effective gene inactivation and generation of specific point-mutation, in-locus gene (fluorescent) tagging approaches, (genome wide) in vitro screening, and improved delivery methods of CRISPR reagents to the target cells.

Resources

CEC has succeeded in creating accessible biobanks of CRISPR reagents, such as plasmids, enzymes, and cell line models. In addition, CRISPR protocols containing validated molecular biology materials and testable controls have been developed, which have been highly rated by collaborating researchers.

CEC has provided consultancy to nearly 100 projects, including 20 outside the CCA, some outside of the Netherlands. It is a co-applicant on numerous grant applications (KWF, EU, ZonMW, and NWO). The center has also recently been granted funding for the acquisition of digital droplet PCR to be used in combination with CRISPR, boosting capabilities.

Towards clinical applications

Recently, resources have been secured to further develop the CRISPR Expertise Center into a support facility serving the broader science community at Amsterdam UMC and beyond. There is great interest from many researchers in utilizing the state-of-the-art whole genome screenings pipeline at CEC. Furthermore, CEC will expand to also focus on the direct application of gene editing applications in the clinic for cell and gene therapy and diagnostic purposes.

CRISPR Expertise Center - Cancer Center Amsterdam

Directors: Dr. Rob Wolthuis (VUmc) and Prof. Louis Vermeulen (AMC)

CEC Manager: Dr. Rodrigo Leite de Oliveira

Assisted Projects: 98

Services:

- Coordinated access to validated reagents, lab protocols, and (primary) cell models suitable for CRISPR gene editing
- Rapid implementation of emerging CRISPR techniques and applications through collaborations and exchange of hands-on know-how
- Outreach, coordination, and education regarding the latest CRISPR developments at Cancer Center Amsterdam and beyond

Education:

- Hands-on personal training
- 6 CRISPR Technology Seminars
- 4 CRISPR User Meetings
- 3 CRISPR introduction courses
- 2 CRISPR courses for the Amsterdam Oncology Graduate School (OOA)

CEC – Cancer Center Amsterdam Publication Highlights

CRISPR KNOCKOUTS, MUTATION CORRECTIONS & NUCLEOTIDE SUBSTITUTIONS

Van Neerven, S.M., et al (2021). Apc-mutant cells act as super competitors in intestinal tumour initiation. *Nature* 594, 436–441.
Outcompeting cancer: neutralizing the super-competitiveness of mutant intestinal stem cells. A totally new cancer hallmark called 'super competition' was identified at Cancer Center Amsterdam using CRISPR cell models developed with support of the CEC.

Glykofridis, I.E., et al. (2021) Loss of FLCN-FNIP1/2 induces a non-canonical interferon response in human renal tubular epithelial cells. *eLife* 10:e61630.
CRISPR/Cas9-mediated gene knockouts were engineered in a non-malignant cell model to perform large scale transcriptomic and proteomic studies providing new insights regarding gene function and oncogenesis.

Van de Vrugt, H.J., et al. (2019) Effective CRISPR/Cas9-mediated correction of a Fanconi anemia defect by error-prone end joining or templated repair. *Sci Rep* 9, 768.
A proof of principle study, correcting a cancer predisposing mutation in cell models by creating frameshifts or designed nucleotide substitutions with CRISPR/Cas9.

CRISPR GENE REGULATION

Blanas, A. et al. (2019) Transcriptional activation of fucosyltransferase (FUT) genes using the CRISPR-dCas9-VPR technology reveals potent N-glycome alterations in colorectal cancer cells, *Glycobiology* 29, 137–150.

CRISPR GENOME-WIDE SCREENS

Buikhuisen, J.Y., et al. (2023) Subtype-specific kinase dependency regulates growth and metastasis of poor-prognosis mesenchymal colorectal cancer. *J Exp Clin Cancer Res* 42, 56. A large CRISPR-Cas9 drop-out screen was performed on 14 subtyped CRC cell lines to uncover essential kinases in all four consensus molecular subtypes of CRC.

Van der Weegen, Y., de Lint, K., et al. (2021) ELOF1 is a transcription-coupled DNA repair factor that directs RNA polymerase II ubiquitylation. *Nat Cell Biol* 23, 595–607.
Discovery of New Genes in DNA Damage Repair by CRISPR Screening Technology at Amsterdam UMC A full-genome CRISPR functional genetic screening pipeline was deployed in Cas9-inducible diploid cells to identify genes involved in DNA damage responses. CCA researchers discovered the previously uncharacterized *ELOF1* gene, an important factor in DNA repair.

CRISPR CANCER DIAGNOSTICS

Kohabir, K.A.V., et al. (2023) In Vitro CRISPR-Cas12a-Based Detection of Cancer-Associated TP53 Hotspot Mutations Beyond the crRNA Seed Region. *CRISPR Journal*.
CRISPR for quick cancer diagnostics: new fundamental insights A research team at Cancer Center Amsterdam is developing a new diagnostic test that can detect cancer-specific DNA mutations quickly, accurately, and cost-effectively.

Appendix 4: Immunotherapy center and Hyperion

The CCA has supported the establishment of an integrated cancer Immunotherapy Center (ITC) in 2022, in which all immunological expertise within the Amsterdam UMC is bundled with the purpose of researching, promoting, and supporting cancer immunotherapy. To achieve this endeavor, the CCA has granted the opportunity to appoint a senior researcher for a period 3 years for coordination, networking as well as internal and external communication. The primary responsibility of the coordinator is to maintain a portfolio of immunological analyses to support translational research and
to bridge researchers and clinicians that are part of the ITC.
The first step for the generation of the ITC was the formation of an executive board, consisting of translational scientist and clinicians performing pre-clinical and clinical research in the immunology and immunotherapy fields. The executive board is committed to strategically guide the decisions and
direction of the center to fulfill expectations and milestones. The establishment of the ITC was promoted via personal discussions between the coordinator and researchers (PIs, Postdocs and PhDs) or clinicians. Overall, the ITC coordinator highlighted 65 potential active members of the ITC and met personally around 50 of them to communicate the concept of the ITC and engage them in its vision. Under the ITC direction two main programs have been initiated since its start at the beginning of 2021. Here a short summary of the goal and structure of the programs followed by a list of supported projects.

- **Immune phenotyping and monitoring pipelines:** The ITC focuses on centralizing and standardizing immune phenotyping and monitoring pipelines. Immune phenotyping and monitoring are an essential tool to identify immunotypes that can correlate with disease progression and therapy response. Cutting-edge technologies are available in our institutes thanks to the presence of an innovative and well-equipped microscopy and flow cytometry facility, nevertheless projects are mostly dependent on individual optimization of protocols. The ITC coordinator worked on the creation of a database that includes optimized panels from researchers that are willing to share their work with potential scientific collaborators. At the moment the database accounts for 13 flow and spectral cytometry, 5 mass[1]cytometry and 20 multiplex immunohistochemistry panels. The database is in continuous expansion and we aim to advertise the presence of this tool to more interested researchers.

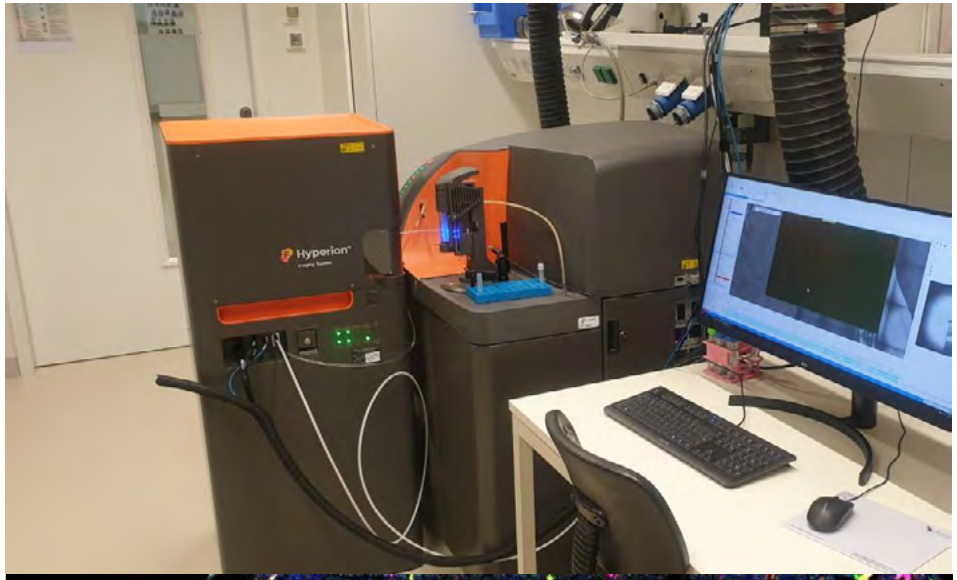
- **Viable Tumor Cell Biobank:** The ITC is responsible for coordinating the development of a viable tumor cell biobank (VTCB). The VTCB was initiate with the aim to collect and store viable primary cells from resected tumor samples. The presence of this biobank gives the possibility to perform functional assays on primary cells, as well as generating innovative model to better reproduce the physiological environment of tumors. Five clinical departments have supported the implementation of the biobank and two of have already started samples collection. At the moment 120 samples have been successfully collected and stored via the VTCB. We aim to increase the number of departments associated to the VTCB and reach 200 samples collected by the end of 2023. Issuance of samples is regulated by a scientific committee.

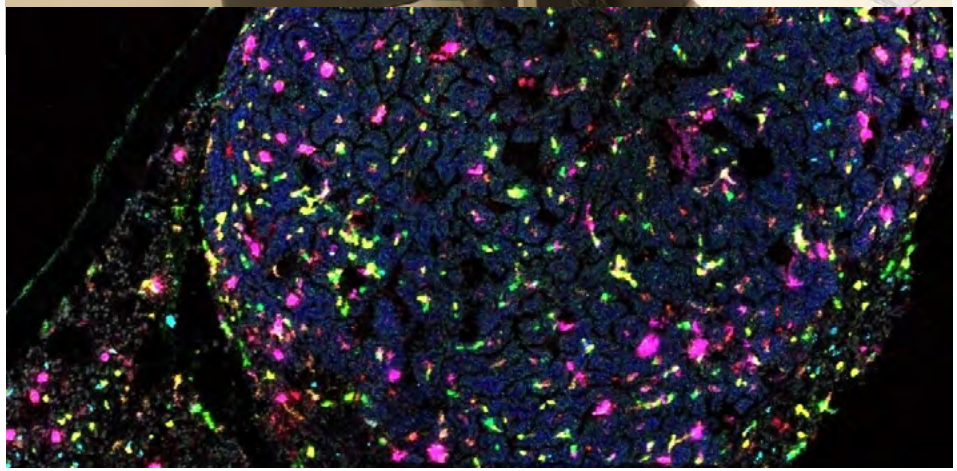
Hyperion at Microscopy and Cytometry Core Facility

The study of the tumor microenvironment (TME) has gained a lot of interest recently because the biological processes that contribute to cancer progression are coupled through a network of spatial interactions between tumor, immune and stromal cells both within the local TME and draining lymph nodes. Consequently, the ability to simultaneously quantify expression of multiple proteins while preserving spatial information at a subcellular level is crucial. To achieve highly multiplexed tissue imaging, mass cytometry has been a key technology in which Cancer Center Amsterdam has invested. Imaging mass cytometry relies on the use of antibodies conjugated to unique metal isotopes, which can be differentiated using mass spectrometry. Antibodies are labeled with metal tags and are then applied to stain the tissue in a single reaction. To obtain spatial information, the tissue is then divided into a dense grid, and the expression of all targeted proteins is read for each pixel using laser ablation time of flight mass spectrometry. The HYPERION allows for rapid evaluation of ~30 distinct proteins in a spatial resolution and thus provides unprecedented protein expression insight into cancer tissue.
Dr. F. Dijk, Dr. Y. S. Kim study the effects of the tumor microenvironment (TME) on pancreatic ductal adenocarcinomas (PDAC)-subtypes, tumor heterogeneity, as well as therapy response and resistance. Considering the importance of PDAC subtypes for treatment and the TME for disease progression and pathogenesis, both need to be better characterized. In order to truly study the effects of the TME in PDAC, current methods are suboptimal, since thus far we have only studied bulk RNAseq, looking at various cell types simultaneously. We can

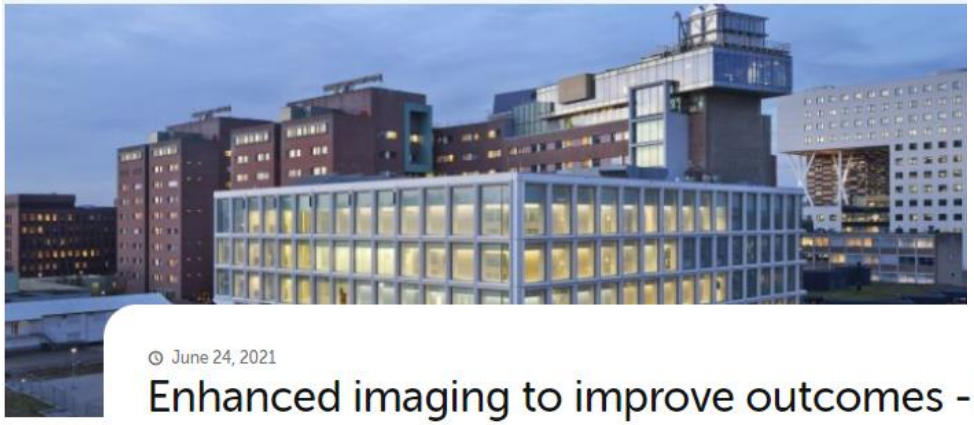
virtually dissect this using the in house developed BLADE-software, however, this has thus far not been validated for PDAC. Therefore in the current study, we will assess whether HYPERION, which enables the simultaneous immunohistochemical staining of ~30 proteins is suitable to deliver comprehensive spatial information on the TME and tumor cells. Using the Hyperion imaging system from Standard Biotools Inc, imaging mass cytometry will be performed, which can subsequently be compared to digital cell type-specific information as obtained through BLADE from bulk RNAseq data from both fresh frozen tissue-obtained tissue as well as from more widely available, but poor quality FFPE-derived RNAseq. So far, we have been working on the design of an antibody panel, which should contain a representative reflection of different cell types that we expect in the PDAC samples, and on the correct dilution of the antibodies. For the selection of antibodies, we discussed with a pathologist, immunologists, biologist and bioinformaticians. For the correct dilution of the antibodies we discussed with the pathologist and with an immunohistochemical expert technician. The majority of the antibodies have been optimized in terms of dilution, using whole mount PDAC tissue slides and as control tissue also colorectal tissue slides. After inclusion of the last few antibodies, we will perform the actual experiments on a tissue micro-array containing untreated and treated PDAC samples.

Dr. F. van Maldegem runs several project running that involve the use of the Hyperion, however these are still in the optimization phase, where we develop the antibody panels before running the actual experimental samples. We have been busy validating panels for mouse and human tissues. The projects that we will use these panels for are: (i) Early tumor-host co-evolution in mouse models of lung cancer; understanding how the tumor microenvironment develops over time and how it evolves under influence of selective events such as T cell recognition. (ii) Necroptosis as selective vulnerability of KRAS-driven pancreatic cancer; A collaboration with a group in Cologne who want to characterize the immune responses in response to loss of necroptosis. (iii) Optimizing radiation dose and immune checkpoint inhibition for human lung cancer; a study of the resected tumor and draining lymph nodes from patients neoadjuvant treated with radiation and immune checkpoint inhibition. The aim is to understand how radiation can support or harm the immune responses in the tumor draining lymph nodes, and how these therapies should be sequenced and dosed for optimal responses.





Appendix 5: Imaging center



June 24, 2021

Enhanced imaging to improve outcomes - Making the invisible visible

Imaging is an indispensable tool for diagnosing, investigating, predicting and treating cancer. Innovations in the field of imaging provide (future) patients and researchers with new opportunities, such as a faster diagnosis or an improved assessment to determine which treatment is most effective.

Diagnose, investigate, predict and treat

The opening of Amsterdam UMC's Imaging Center on location VUmc, where ultra-modern imaging facilities are gathered together under one roof, was a huge leap forward for patients, practitioners and researchers.

No patient is the same. That is why it is so important to get an accurate picture of the course of the disease in an individual. Opened in 2019, the Imaging Center of Amsterdam UMC offers technical facilities that provide a good diagnostic picture, and brings together clinical care, research, and drug development under one roof. That means more benefits for both the patient and the researcher. Guus van Dongen, professor of Medical Imaging and founder of the Imaging Center was recently awarded the prize for the best basic science article in 2020 and the overall best article in 2020 by the Journal of Nuclear Medicine. Read more about these awards on the website of the society of nuclear medicine & molecular imaging.

Treatment and research under the same roof

The Imaging Center is a unique and remarkable facility. It is the only place in the world where production, treatment and research are brought together in one center. This is where the most advanced medical imaging techniques for healthcare and scientific research come together with the latest techniques in the field of diagnostics. "Being in one place allows us to diagnose faster and see which treatment is best," said Guus van Dongen, professor of Medical Imaging and founder of the center.

> *"Above all, the Imaging Center is a place where we can treat patients in the best and fastest way in the most pleasant environment possible."* Guus van Dongen, professor of Medical Imaging.

More affordable plus improved patient care

Because the Imaging Center hosts both medical and pharmaceutical research, the costs of drug development can be reduced. Treatments become more targeted: the right treatment for the patient can be administered at the right time. In addition, the center has an important international role in drug development and cost control. "In the Imaging Center, we make the medical isotopes and tracers for other Dutch hospitals and foreign research centers in an environmentally friendly way," says Van Dongen. "But here too, patient care remains paramount," he continues. "Above all, the Imaging Center is a place where we can treat patients in the best and fastest way in the most pleasant environment possible."

Bert Windhorst, professor of Radiopharmaceutical Chemistry at Amsterdam UMC, received a European grant of 30 million euros to conduct research into the effectiveness of immunotherapy. He will conduct the research at the Imaging Center where it is possible to visualize immunotherapy dynamics using non-invasive and high-end imaging techniques. With the development of 'tracing substances', it can be determined whether immunotherapy is promising for a patient. This groundbreaking research would not have been possible without the Imaging Center.

Joining forces

The aim is to develop new imaging techniques, tracers, methods and medicines in order to improve healthcare for all. The project was awarded a grant of 30 million euros from the Innovative Medicines Initiative (IMI), a joint technology initiative of the European Union (EU) and the European Federation of Pharmaceutical Industry and Associations (EFPIA). The endeavor, launched on October 1, 2019, brings together ten European top scientific institutions, seven pharmaceutical companies, four small- to medium-sized companies, and one patient organization. This type of cooperation characterizes our chosen course in the fight against cancer: progress can only be made by joining forces and expertise.

Read more about this project and the current state of affairs: immune-image.eu

[credits]

The header image was made by William Moore, Wiegerinck architecten

Part of this text was derived from the article "Looking at what drugs are doing in patients" by Daniëla Cohen. Read the original article here

Appendix 6: Liquid Biopsy Center

The Liquid Biopsy Center (LBC) was established in 2017 from a generous €1.5M subsidy granted by the *Cancer Center Amsterdam* foundation. As central facility within *Cancer Center Amsterdam,* LBC aims to advance and expedite liquid biopsy-related cancer research initiated by Cancer Center Amsterdam researchers. It does so by centrally coordinating liquid biopsy biobank projects in collaboration with clinical departments, the clinical chemistry department and the central biobank facility at both Amsterdam UMC locations. LBC offers hands-on support in the initiation and management of biobank projects to comply with legal-ethical requirements, harmonized processing and storage protocols for the collection of high-quality biofluidic samples, clinical annotation of samples for overview in a sample catalogue, and swift retrieval of samples for use in research projects. For the collection of samples from patients with earlier stage disease, LBC collaborates with hospitals in the Noord-Holland and Flevoland region. This unique centralized setup has resulted in a large cross-CCA biobank of longitudinally collected, high-quality and well-annotated samples from patients with different forms of solid and hematologic cancers. All samples are available to cancer researchers. For this, LBC has installed a scientific board to review sample requests on scientific value and fair use of samples. Several innovative scientific research projects already made use of LBC samples and 26 projects have been published in peer reviewed journals so far. Given the uniqueness of its setup and the vast, clinically annotated sample collection, LBC will be instrumental for development and validation of patient-friendly, non-invasive methods (liquid biopsies) to detect and diagnose cancer and recurrence early-on as well as to monitor therapy response and guide clinical decision making in a cost-effective way.

Numbers of users/projects (table)

In the period 2017-2023, an increasing number of projects teamed up with LBC (refer to table). In total, 17 biobank projects initiated from 7 clinical departments (pulmonary diseases, surgery, medical oncology, gastroenterology, hematology, radiotherapy and internal medicine) actively contributed to LBC. A total of 8,008 samples were collected from 4,055 patients suffering from different tumor types such as lung cancer, colorectal cancer, liver cancer, pancreatic cancer, head and neck cancer, melanoma and lymphoma. At the same time, the number of received requests for the use of biobank samples in research projects as well as the number of issued samples have both increased to 46 requests and 1,599 issued samples by the end of 2022.

Successes

- Unique in its central and hands-on setup within The Netherlands.
- 17 associated biobank projects from 7 clinical departments across both Amsterdam UMC locations.
- Collection of 8,008 samples from 4,055 patients and healthy donors.
- All samples are of equal and comparable high quality due to centralized logistics.
- Automated clinical annotations from the electronic health record in pilot phase.
- Active collaborations with two hospitals (OLVG and Dijklander Ziekenhuis), with three other hospitals in preparation.
- Active *spouse program* for the collection of age- and lifestyle matched control samples.
- Active use of biobanked samples for research projects by cancer researchers from *Cancer Center Amsterdam* as well as external cancer researchers.
- High biobank turn-over rate of 18.5% where <10% is average for biobanks internationally.
- 26 scientific publications resulting from LBC samples and/or scientific support.

LBC project	Tumor type	Principal Investigator	Department	Initiation Year	#patients	#samples
LBC thoracic oncology	Lung & thoracic	Idris Bahce	Pulmonary diseases	2017	866	2274
Bio-HPB	Hepatopancreatobiliary	Maarten Bijlsma	Gastroenterology	2018	1437	1681
LBC colorectal cancer	Colorectal	Jurriaan Tuynman	Surgery	2018	365	683
BioHEP	Liver & bile duct	Bart Takkenberg	Gastroenterology	2019	363	514
BioPAN	Pancreatic	Maarten Bijlsma	Center for Experimental and Molecular Medicine	2019	84	85
Healthy donors AMC	-	Jörg Hamann	-	2019	125	125
LBC head and Neck cancer	Head & Neck	Jens Voortman	Medical Oncology	2019	51	120
LBC melanoma	Melanoma	Tanja de Gruijl	Medical Oncology	2019	104	165
HOVON902	Lymphoma	Martine Chamuleau	Hematology	2020	250	1766
LBC bladder carcinoma	Bladder	Jens Voortman	Medical Oncology	2020	54	72
LBC hematology	Hemato-oncology	Canan Alhan	Hematology	2020	5	5
BIOES	Esophageal-stomach	Hanneke van Laarhoven	Medical Oncology	2021	331	490
LBC spouse	-	Idris Bahce	Pulmonary diseases, surgery	2021	6	6
LBC breast Cancer	Breast	Desirée van den Bongard	Radiotherapy	2022	*-Starting up-*	
LBC endocrine tumors	Endocrine	Koen Dreijerink	Internal Medicine	2022	14	22
IOB	Immuno-oncology	Adriaan Bins	Medical Oncology	2023	*-Starting up-*	
LBC palliative care	End stage solid tumors	Zita Kruise	Medical Oncology	2023	*-Starting up-*	
+ 17 projects					+4,055	+8,008

Appendix 7: ADORE

Stimulating collaboration and knowledge sharing between neurology and oncology researchers

ADORE stands for Amsterdam Oncology and Neuroscience Research. It is a bold, new approach to scientific medical research based on exploring the parallels between oncological and neurological diseases. ADORE means research with international ambitions, performed in an outstanding building equipped with unique scientific technology and infrastructure.

ADORE is a collaboration between two leading research institutes of the largest university medical center in the Netherlands, Amsterdam University Medical Centers, namely Cancer Center Amsterdam and Amsterdam Neuroscience, involving more than 2.000 researchers. In this collaboration, our cancer and neuroscience researchers join forces to discover new insights and accelerate the development of new treatments for people suffering from cancer and nervous system diseases such as Alzheimer's or Multiple Sclerosis, which can have an enormous impact on patient's lives and their loved ones.

Unique collaboration between oncology and neurology

This collaboration is unlike anything else in the world today. At the same time, it is also very logical. Prof. Geert Kazemier, surgical oncologist, Director of Cancer Center Amsterdam Foundation, and one of the initiators of ADORE: *"We want to achieve a better understanding of why human cells start to multiply explosively, causing cancer, and why other human cells simply start to die in diseases such as Alzheimer's or Multiple Sclerosis. Due to the cross-pollination between our researchers, we aim to achieve breakthroughs in science faster. I strongly believe that the steering mechanisms of cell growth and cell inhibition in the two disease areas are overlapping. And if you manage to identify that, you achieve two aims at once: on one hand you will help the neurological patient and on the other hand the oncological patient."*

Ultimate meeting place with shared facilities

> *"We are good at spotting new talent. If you put all the talent together in one place and give people the opportunity to develop, great things will happen. That takes courage, but the likelihood of a paradigm shift is also high."*
> Prof. Jan Paul Medema, Scientific Director Cancer Center Amsterdam

A new *state-of-the-art* research center is being built right behind the hospital next to the world-class Imaging Center. The ADORE/RDC building will offer a pleasant working environment created to enhance serendipity. It will be the ultimate meeting place for top researchers, a breeding ground for discoveries and scientific talent. Researchers in oncology and neurology will work alongside one another, making optimal use of shared state-of-the-art facilities. By learning from and inspiring each other, we will unlock new insights. It is precisely through this cross-pollination of disciplines that innovations and breakthroughs can be achieved in the fight against these diseases.

More than a building

ADORE is, however, more than just a building. It is a concept: a unique environment for doctors, patients, and researchers in oncology and neuroscience where diagnostics, imaging, research, and care join forces. This concept interconnects the entire campus of the Vrije Universiteit Amsterdam, including the Imaging Center, O2 building, Immunotherapy Center, and the new bèta medical lab building.

Whole Body PET-CT scanner in the Imaging Center

The ADORE Research Fund also aims to attract and retain exceptional talent by guaranteeing research funding for up to 10 years. This allows top researchers to focus their time and energy on their work and promotes a stable and fertile research environment. The world's best researchers will be free to pursue unique and ground-breaking research for a meaningful period of time.

Translational research

The location of the ADORE research building next to the hospital provides the indispensable key to translational research. A continuous exchange and review of knowledge and ideas between the scientists in the laboratories and doctors and patients in the clinic allows us to bring research-based knowledge into policy and practical care quickly and safely, while pressing clinical needs can be easily translated into research questions to improve patient care.

We believe that the best results in the fight against cancer and neurodegenerative disorders are achieved when the patient's voice and experience are integrated into the research. This requires a physical environment that enables this to happen; the Atrium, for instance, will allow patients, doctors, and researchers to mingle. This greatly enhances the exchange of ideas and knowledge, helping us to look beyond the boundaries of specific disorders, roles, and medical specialties.

Artist impression by Studio Hartzema. The Atrium

Costs and Financing

To make ADORE possible, a budget of €100 million is required over a period of 10 years. The initial extra investment of €30 million for the construction of the building costing a grand total of €106 million has nearly been completed by the ADORE Investment Fund. An additional €70 million spread over 10 years is needed to enable scientific operations. The ADORE Research Fund has been set up to achieve this, providing €7.0 million per annum over a period of 10 years.

This fund will be used to attract and retain the very best scientific talent over the long term and enable us to make the breakthroughs that we are aiming for.

'It appears that people with Alzheimer's are less likely to get cancer. And conversely, people with cancer have a smaller chance of developing Alzheimer's. That's a puzzle that I want to get to the bottom of! My dream is to use that knowledge to find a solution for Alzheimer's.'
Prof. Wiesje van der Flier, Scientific director of Alzheimer center Amsterdam at Amsterdam UMC

ADORE IS UNIQUE

A breakthrough in research

Within ADORE, everyone is working towards the same goal: achieving research breakthroughs in the fight against cancer, Alzheimer's, and Multiple Sclerosis.

Breaking through traditional boundaries

At ADORE, we are exploring new territory by breaking through the traditional boundaries between the worlds of oncological and neuroscientific research.

Translational research

Translational research plays a central role at ADORE: there is constant interaction between the outpatient clinic, the hospital, and the research laboratory. This allows our patients to benefit directly from the latest treatment methods and informs and inspires our research.

10 years of research, guaranteed

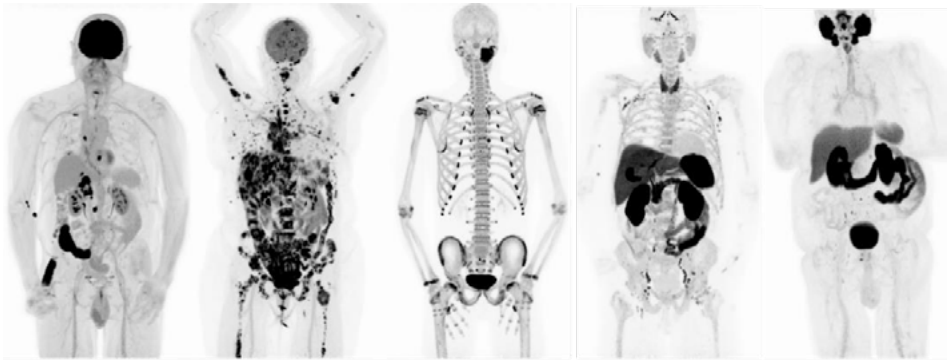
At ADORE, we guarantee 10 years of funding for world-class researchers.

Two Amsterdam UMC institutes

At ADORE, two leading Amsterdam UMC institutes work together in a unique partnership: Cancer Center Amsterdam and Amsterdam Neuroscience.

Appendix 8: Full body PET-CT

A quantum jump in imaging technology



The acquisition of a unique new 'total body' PET-CT system at the Imaging Centre of the Amsterdam UMC, one of only a handful currently available globally, is offering opportunities to dramatically expand both clinical and scientific horizons. The new imaging system propels Cancer Center Amsterdam into position as a global leader in pioneering new therapies, developing breakthrough procedures, and facilitating novel diagnostics.

PET-CT scanners generate quantitatively accurate 3D distributions of an infused/administered radioactive tracer. By using different radioactive tracers, it allows visualizing of various biological information in the body. With precise and detailed pictures of organs and tissues, PET-CT imaging technology has revolutionized medical diagnosis and advanced precision medicine over the last 20 years.

New: Biograph Vision Quadra total body PET-CT system

The new Biograph Vision Quadra from Siemens Healthineers is a groundbreaking imaging system that is a quantum jump forward in PET-CT technology.

What does it do better than standard PET-CT scanners?

✓ **Larger field of view**

The radioactive tracer used in PET scans is administered to a patient and spreads throughout the entire body. However, traditional PET-CT scanner's axial field of views are only up to about 25 cm, meaning that dynamic tracer uptake can only be followed in a small portion of the body.

The Quadra system is much larger with a 106 cm axial field of view. This unique scan length covers ~85% of the body volume, allowing a view from the top of the head to mid-thigh on an average adult. This 'whole-body' range encompasses all the critical organs

Radiotracers

PET imaging is playing an increasingly important role in drug development, as it provides valuable evidence on target engagement and off-target binding through the use of radiolabeled drugs (tracers) such as small molecules, antibodies, immune checkpoint inhibitors, bispecific agents, and nanoparticles. Fluorine-18 (18F) and Gallium-68 (68Ga) are commonly applied short-lived radioisotopes that are linked to these bioactive compounds. PET-CT imaging is used for patient selection, drug treatment response prediction and monitoring, and personalizing therapy. Moreover, new tracers for emerging targets - such as immune cell subsets to monitor immune response - are under development at Cancer Center Amsterdam.

mostly evaluated in molecular imaging studies.

"The system enables us to image all major organs at once, immediately after administration of the radiotracer. This is the most important breakthrough," explains Ronald Boellaard, Professor, Radiology and Nuclear Medicine. "Never before has it been possible to follow radiotracer uptake dynamically and continuously over all critical organs in the body. Because we can do this now, we get a lot more information and we can do much more extensive analyses."

✓ **Ultrahigh sensitivity & lower radiation exposure**

Covering more anatomy in one scan position also directly increases sensitivity by capturing more of the radioactive signal. The sensitivity of the Quadra is about 10 to 20 times higher compared to current state-of-the-art PET/CT systems.

The higher sensitivity and wider view mean that much less radiation is needed. "Using less radiation opens the door to doing more frequent and/or multi-radiotracer repeated PET-CT scans to allow follow-up investigations or a more comprehensive biological characterization of organs, such as the brain, or tumors," says Prof. Boellaard.

✓ **Huge potential for patients and research**

Advantages offered by the new system include, but are not limited to:

- Earlier and better detection and diagnosis of cancer or neurodegenerative diseases,
- Investigation of cell-based therapies including trafficking patterns,

- A more comprehensive (whole body and multi-radiotracer) investigation or characterization of oncological and neurological diseases, among others (*i.e.* inflammation)
- Acceleration of new drug development,
- Rapid clinical deployment of new therapeutic agents.

Strategic Investment: on site 68Ga isotope generators

The application of radioactive gallium (68Ga) greatly facilitates the (pre)clinical development of novel tracers visualized by PET imaging. However, the equipment and infrastructure to generate 68Ga were not available at Cancer Center Amsterdam. An investment budget enabled an initiative by professors Ronald Boellaard and Bert Windhorst to purchase 68Ga generators and establish good medical practice procedures to implement new tracer molecules for improved imaging and diagnosis of specific lung tumors, pancreatic cancer and other malignancies.

"We have already established the radiolabeling of 68Ga-FAPI-046 (targeting FAP), 68Ga-NOTA-CD206-VHH (nanobody targeting CD206), 68Ga-exendin (peptide targeting GLP1) and are working on the radiolabeling of 68Ga-TUNA (peptide targeting GRRP) as well as 68Ga-pentixafor (peptide targeting the CXCR4)," says Prof. Boellaard. Preclinical studies focusing on immune cell tracking in vivo can now be realized to develop more effective therapies against cancer.

Several promising studies are underway using novel gallium tracers. These tracers (called [68Ga and 18F]Ga-FAPI-46) have shown great potential for detecting pancreatic, bile duct, rectal, and breast tumors that are not easily detectable with the commonly used sugar tracer, 18F-FDG. However, essential knowledge about factors such as tumor perfusion, clearance/excretion, and the effect of certain drugs on the behavior of this promising PET tracer was needed before it can be routinely used for both clinical care and scientific research.

More than promising

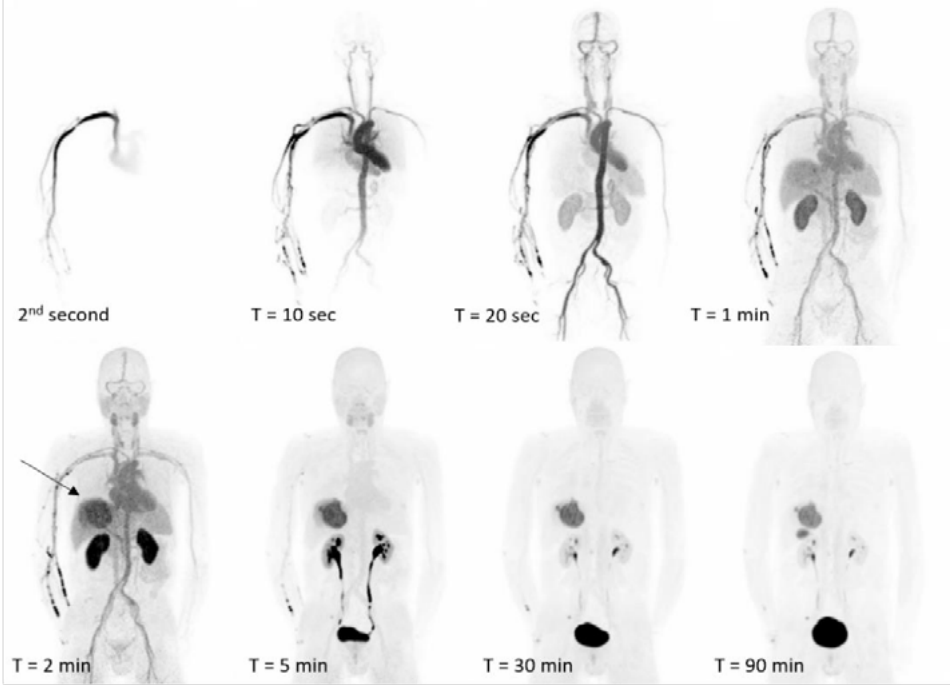
The Quadra has been in use since mid-May 2022 and currently there are 12 oncology imaging studies ongoing with the Whole Body PET/CT.

"While it is too early to draw definitive conclusions, the high spatial and temporal resolution of dynamic whole-body scans are impressive and initial findings are more than promising," says Ben Zwezerijnen, a medical specialist in radiology and nuclear medicine at Cancer Center Amsterdam.

The first whole-body dynamic [68Ga]Ga-FAPI-46 PET scan in a patient with bile duct cancer. The arrow indicates the location of the tumor, which becomes visible 2 minutes after the administration of the tracer.

Already making an impact on clinical care

According to Prof. Boellaard, the Whole Body PET/CT scanner has already made a significant impact on clinical care. Due to its high sensitivity, patients are now scanned with lower tracer doses (i.e., less radiation) and in a much shorter time (8-10 minutes versus 25-40 minutes on a conventional PET camera), while still achieving significantly higher diagnostic quality.



"The total body PET-CT system empowers researchers at Amsterdam UMC to be amongst the world's leaders in molecular imaging and ensures our patients are receiving world-class management of their conditions." Ronald Boellaard, Professor PET methodology, Cancer Center Amsterdam.

Funding

The Amsterdam UMC Imaging Centre and the total body PET-CT system are made possible because of contributions from the European Regional Development Fund (ERDF), the City of Amsterdam, the Department of Economic Affairs of the Netherlands, and the Province of Noord-Holland. It is actively supported by Amsterdam Economic Board and Amsterdam Marketing, Kansen voor West. In addition, the total body PET-CT system, part of the Innovatiecentrum ADORE project, is financially supported by the Amsterdam Oncology and Neuroscience Research (ADORE) institute'.

Appendix 9: PoC, bench to bedside stories

> We believe that MI therapy may overcome resistance to immunotherapy in patients with melanoma.
>
> Dr. Mariette Labots — Medical Oncologist

April 5, 2023

Bench to bedside / Can we overcome resistance to immunotherapy in melanoma patients?

In light of its mission to intertwine research and care, Cancer Center Amsterdam Foundation funds Proof of Concept (PoC) / Proof of Principle (PoP) projects to translate promising preclinical research findings from Amsterdam UMC researchers into early clinical studies. The study proposal from patient research group of Dermato-oncology was one of two projects selected for funding. The phase Ib study will assess the combination of a new therapy with existing immunotherapies to improve outcome for patients with advanced melanoma.

Melanoma is a type of skin cancer that can spread quickly to other parts of the body, making it difficult to treat. Traditional treatments such as chemotherapy and radiation have only limited success in treating advanced melanoma.

More recently, immune checkpoint inhibitors (ICI), a type of cancer immunotherapy, have revolutionized the treatment of advanced melanoma by unleashing the power of the immune system to attack cancer cells. But ICI therapy does not work for all patients, possibly due to the lack of pre-existing antitumor immunity or acquired tumor resistance.

Joining Forces

"Analyses by our group and others have shown that the development of auto-immune skin depigmentation - or vitiligo - during immunotherapy was significantly associated with prolonged survival of advanced melanoma patients," says Rosalie Luiten, professor of Experimental Dermatology.

Based on that observation, the group developed MI therapy. MI therapy combines the vitiligo- inducing agent monobenzone with imiquimod, which induces melanoma-specific immunity and melanoma regression in preclinical models and patients. This project will translate these (pre)clinical findings further to the clinic by combining the expertise of oncologists Dr. Mariette Labots and Prof. Fons van den Eertwegh, with immunologists Prof. Rosalie Luiten and Prof. Tanja de Gruijl, head of the Immunotherapy Lab of the Department of Medical Oncology, at Cancer Center Amsterdam, as well as collaborators in participating centers NKI-AVL and LUMC.

Paving the path for clinical application

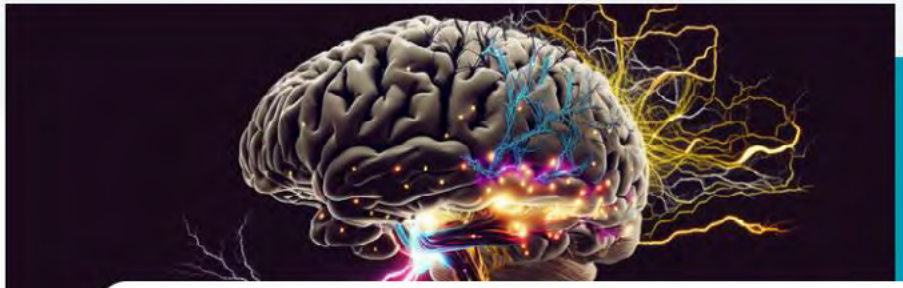
The funded project will test MI therapy in combination with ICI.

"We think that MI therapy may potentiate immunotherapy and contribute to overcoming resistance in patients with melanoma," says Dr. Labots. "By adding MI therapy to ICI, we will induce specific anti-melanoma immunity, which will be amplified by immune checkpoint inhibitors. So MI therapy can be a potentiator of ICI efficacy in melanoma patients to improve the clinical benefit."

Preliminary work by the Luiten group has shown that MI therapy alone is a low-cost, broadly applicable, and well-tolerated treatment that induces local and systemic anti-melanoma immunity and local tumor regression.

The phase Ib clinical study will assess the safety and tolerability of the combination of ICI with MI therapy, in addition to determining the maximum tolerated dose. The results are expected to provide proof of principle for a subsequent Phase II efficacy evaluation in patients with melanoma metastases.

For more information contact: Dr. Mariette Labots or Prof. Rosalie Luiten.



April 20, 2023

Bench to Bedside / Early clinical study will test an 'electrifying' new therapy to fight aggressive brain tumors

In light of its mission to intertwine research and care, Cancer Center Amsterdam Foundation funds Proof of Concept (PoC) / Proof of Principle (PoP) projects to translate promising preclinical research findings from Amsterdam UMC researchers into early clinical studies. The study proposal from the tumor research group of Neuro-Oncology was one of two projects selected for funding. This project will investigate the safety and effectiveness of direct electrotherapy using deep brain stimulation (DBS) electrodes as a novel treatment strategy for glioblastoma, an aggressive brain cancer with a poor prognosis.

Glioblastomas are an aggressive form of brain cancer. Despite intensive research, treatment options remain limited and prognosis for patients is poor, with a life expectancy of only 14 months.

A Cancer Center Amsterdam Foundation-funded PoC/PoP project from Neuro-Oncology is bringing together clinical and preclinical researchers to investigate the safety and effectiveness of a novel approach for glioblastoma treatment: direct electrotherapy using deep brain stimulation electrodes. Project leaders are Lucas Westerink and Natalia Goriounova, and research team members include Philip de Witt Hamer, Linda Douw, Bart Westerman, Pieter Wesseling, David Noske, Martin Klein, Rick Schuurman, Pepijn van de Munckhof, and Matthew Hebb (Canada).

A stronger effect on glioma tumor cells

"The idea is that inducing electrical fields by deep brain stimulation will inhibit glioma cell division by preventing alignment of essential cell structures. It also makes cell membranes more porous which could enhance drug delivery," says Lucas Westerink, physician in Department of Neurology and Neurosurgery.

The study will combine preclinical investigation of biological mechanisms and optimal settings of the treatment in ex vivo glioblastoma models with a clinical safety study in patients. This allows for a better understanding of the potential benefits and risks of the therapy before moving into larger clinical trials.

> "We are hoping to see a long-term synergy from electrotherapy and drug combinations.
>
> Natalia Goriounova — Assistant Professor

> "We think that by applying deep brain stimulation using implanted electrodes, we can have a stronger inhibiting effect on the tumor.
>
> Lucas Westerink — Physician in Department of Neurology and Neurosurgery

'Zapping' brain cancer cells

Electrotherapy using a portable, non-invasive device that transmits low-intensity electrical fields through the scalp and into the brain has already received approval (US FDA) for glioblastoma treatment. This device induces apoptosis (cell death) and inhibition of mitosis in cancer cells, although the precise mechanisms of action are unclear. However, the non-invasive device has several drawbacks including the need for a shaved head, frequent electrode changes, scalp complications, external device stigmata, and inability to target deep-seated disease. The researchers hope to overcome these limitations by implanting stimulating electrodes directly in the brain.

"We think that by applying deep brain stimulation using implanted electrodes, we can have a stronger inhibiting effect on the tumor," says Lucas Westerink. "DBS with implanted electrodes is already a known effective and safe therapy for neurological diseases like Parkinson's disease."

Potential for combination therapy

The study will also investigate the potential for combining electrotherapy with compound inhibitor drugs to improve treatment outcomes for patients. This could lead to the development of new treatment strategies for glioblastoma that target multiple pathways.

"We'll start by testing drug combinations identified in the lab of Bart Westerman (using the drug-atlas concept) in a model system made from cultured glioblastoma tissue that was established in my lab," says Natalia Goriounova, assistant professor in the Department of Integrative Neurophysiology, Center for Neurogenomics and Cognitive Research (CNCR), Vrije Universiteit Amsterdam. "We are hoping to see a long-term synergy from electrotherapy and drug combinations. Some of the drugs we will be testing have a poor blood-brain barrier penetrance potential and are therefore expected to be candidates for more effective delivery due to the electric fields."

Bench to Bedside

"While there is still much work to be done, this early clinical study has the potential to revolutionize the treatment of glioblastoma and showcases the important role that bench-to-bedside research can play in advancing cancer care," concludes Lucas Westerink.

Appendix 10: CCA Ambulatory Patient outcome assessment Platform CCA-APP

Online symptom monitoring in cancer care is associated with better quality of life, less emergency room visits, longer overall survival and is a cost-effective approach (Basch et al. JAMA. 2017; Denis et al. JNCI 2017; Lizée et al. J Thorac Oncol 2019). However, absence of starting budget, integration in electronic health records, and local success stories hamper implementation in clinical research and practice. For the CCA-APP project, the overall goal was to make a symptom monitoring application available for scientific research and clinical practice for cancer patients. Objectives included creating support, application selection, METC application, validating content, user experiences and scientific evaluation.

Strategic choices

In order to make the CCA-APP project a success, we have made two adamant strategic choices. First, we chose to start the project in an area wherein many research initiatives were present, and where supportive care was not fully operable in clinical practice, i.e. immunotherapy for cancer patients. We worked together with clinicians and researchers to develop a core set of symptoms to monitor over time, which qualified as an unmet need.

Second, we chose the KLIK application over other available providers, because of the integration with our electronic health records provider EPIC. This limited our scope, as we could not add wearable technology in this application, but trained clinicians received immediate feedback on their patients symptoms and wellbeing in their medical files. The additional value of wearable technology on top of patient reported outcomes was tested in parallel projects (CAMP-IT, Follow that CAR, and eBLADDER).

Initiated projects

After a long run-up with changes in the project team, a KLIK application is in use in the Amsterdam UMC, which is available for scientific research and clinical care, including a link with EPIC, our electronic health records system. The application allows patients and healthcare professionals to monitor symptoms during the treatment period. Patients enrollment is completed and results are being analyzed and reported.

The symptom monitoring is based on the CTCAE list and has been prepared for online monitoring in immunotherapy together with involved clinicians. The symptom list is already being used in another project (CAMP-IT), as well as the methodology used in another cohort of patients with hematological malignancies who are treated with CAR T-cell therapy (Follow that CAR).

The project focuses on remote care and can be rolled out throughout the region, which fits in with the objectives of Cancer Center Amsterdam, as well as in the strategy of the 'Samen Digitaal' program from the outpatient clinics of Amsterdam UMC.

Successes

At the end of the project, all objectives have been achieved, with a clinically validated symptom monitoring app integrated into EPIC.

Publications listed below have come out of the project, and pending the analyses of results two publications directly from CCA-APP and others will follow from adjacent projects.

1. Kampshoff et al. Ecological momentary assessments among patients with cancer: A scoping review. Eur J Cancer Care 2019
2. Kos et al. The association between wearable activity monitor metrics and performance status in oncology: a systematic review. Supportive Care Cancer 2021
3. Stuijt et al. Potential Role of Smartphone-Based Passive Sensing in Remote Monitoring of Patients With Cancer. JCO Clin Cancer Inform 2022
4. Kos et al. The association between wearable device metrics and clinical outcomes in oncology: A systematic review with evidence synthesis and meta-analysis. Crit Rev Oncol Hematol. 2023
5. Spanjaart et al. Development of a Core Set of Patient- and Caregiver-Reported Signs and Symptoms to Facilitate Early Recognition of Acute Chimeric Antigen Receptor T-Cell Therapy Toxicities. JCO Oncol Pract 2023

Follow-up funding has been obtained for the CAMP-IT study with the VIDUET platform, wherein 50 patients were enrolled in 4 hospitals, including Amsterdam UMC. In addition, funding has been obtained for the Follow that CAR study with the Luscii platform in collaboration with hematology. Together with Center for Human Drug Research, a grant was obtained from KWF for eBLADDER study, using the Trial@home platform in patients undergoing multimodal therapy for bladder cancer in Amsterdam UMC and LUMC. First patient was included in January 2023. Finally, in April 2023, a large consortium grant has been submitted to KWF for the clinical validation of the CAMP-IT study.

Appendix 11: Grant support

Acquiring research funding has become increasingly complex due to the use of topic-specific calls for proposals by funding agencies, which limit resources for curiosity-driven fundamental research and increase competition. Additionally, strong emphasis is placed on large-scale consortium projects, with selection criteria that go beyond scientific excellence to include social and economic impact, implementation, and dissemination of findings. European calls for proposals often contain global terms, making it necessary to carefully analyze work program documentation to determine if a call matches a researcher's plans. This can be challenging for scientists who lack time and expertise.

To address this issue, Amsterdam UMC offers grant advice through Research Grant Support (RGS), which provides support for prestigious personal grants, including the NWO talent scheme and ERC grants, as well as HORIZON Europe consortium projects. To further support funding opportunities in the oncology field, Cancer Center Amsterdam has employed a dedicated grant advisor. Although the previous advisor's position was not replaced due to financial reasons, funding support remains one of the most frequently requested services from Cancer Center Amsterdam.

Cancer Center Amsterdam has now attracted a new grant advisor who will focus on identifying oncology-relevant funding opportunities, reviewing project proposals, and talent scouting. The advisor will share new funding opportunities through a biweekly Cancer Center Amsterdam newsletter and a funding calendar on the website. They will also perform grant scans for individual cases and link researchers to relevant calls. The advisor will work in close collaboration with Amsterdam UMC RGS grant advisors and follow relevant courses and workshops to gain experience in various grant structures. The main role of the advisor is to support researchers in their grant applications. The first stage of this is to identify funding organizations and grant opportunities and assemble a calendar with descriptions and deadlines.

There are many funding opportunities besides the well-known Dutch Cancer Society or Dutch Research Council that our researchers need to know about. For example, the European Union (EU) offers many different types of research funding. These programs are often less visible and application procedures can be cumbersome. Support to navigate this maze of EU grants and inform researchers of relevant funding opportunities s crucial.

Finally, the grant advisor will stand in close contact with Cancer Center Amsterdam researchers to identify talented researchers and provide personal career advice. They are part of the centralized Amsterdam UMC working group on talent management, which develops a database to aid in the nomination of talented researchers for national and international awards.

Grant support officer Wietske Pieters

Overall, the Cancer Center Amsterdam grant advisor offers accessible and personalized funding advice to researchers in all career stages

Appendix 12: Business development

Business developers' role:

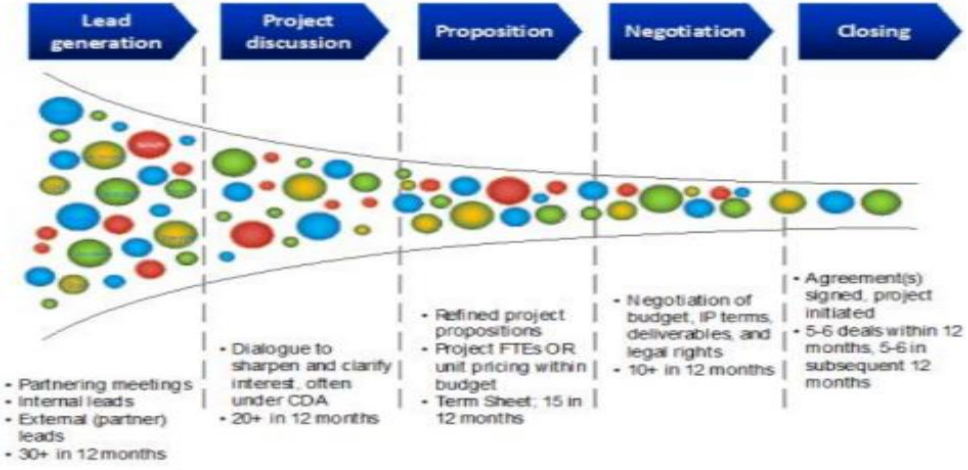
Advising and assisting researchers to create economic and societal impact with their research is the main role of the Business developers at Cancer Center Amsterdam. From the moment a CCA researcher has made a discovery or invention, we help him/her in bringing this invention to the patient. This can be done by organizing investors and a team to start a spin-off company to further develop this invention, or by licensing the invention to an existing company having the right expertise and infrastructure to bring the invention to the patient, in the form of a new treatment or application.

Besides inventions, we stimulate researchers to collaborate with industrial parties such as biotech, pharma and med tech companies. This can be any type of collaboration, such as:

- Research projects (pre-clinical or clinical)
- Public-private-partnership grants (eg TKI-PPS)
- Investigator initiated trials
- Consultancy activities for the company

-Material transfer agreements

Industry collaboration projects



We negotiate the main terms of these collaborations and provide financial expertise. Since mid-2021, we are also proactively reaching out to companies to explore opportunities for mutually beneficial collaborations.

Finally, we aim to increase "valorization awareness" amongst CCA researchers. We do this by giving presentations on the importance of valorization and by urging researchers to reach out to us when they have interesting findings or when they are or wish to be approached by companies.

Strategic choices:

Dedicated business development for Cancer Center Amsterdam was kicked off in 2019 by IXA and CCA, with the main aim to create a single point of contact for CCA researchers in need of valorization support. During 2021, a second business developer was hired. In addition, 2 valorization officers were appointed to give strategic direction and daily guidance to both Business developers. This led to narrowing the focus areas for active valorization support to immunotherapies, especially cell &gene therapies; drug screens & target finding; predictive modelling & biomarkers. Furthermore, it was noted that most valorization activities were conducted by a relatively small group of PI's. To show that dedicated BD support could be made sustainable, a "valorization team" of 25 such PI's was formed and a financial model was developed. In short, this financial model implies that a dedicated BD fee is charged to the company on all collaborations with companies that receive full-service project support. A pilot on the feasibility of this financial model is currently ongoing during 2023. In case of a positive outcome, it will be extended during 2024-2025 to also provide funding for back-office and legal support. Any remaining funds will be used to finance new high-risk high-gain research within CCA.

To improve visibility of all CCA researchers and not limit this to the "valorization team", it was recently decided by the CCA Board to provide pro-active assistance in completion of "Pure" and/or other means of online media attention. This will be executed during Q2 and Q3 2023.

Business development key successes

Overview in numbers

Performance indicator	**# (2017-2022)**
license deals based on CCA IP*	6
CCA inventions filed as patent*	30
Research collaborations*	132
Collaboration opportunities through BD (quarterly since 2021)	10
AUMC TKI-PPP grants (300-750k euro per project)	12

*As the registration in IXA database does not include institute, numbers are based on the "CCA valorization team" PI's

License deals – creating impact from CCA knowledge transfer

Company	**PI**	
Cimcure	Arjan	Griffioen
Skyline	Thomas	Wurdinger
ViewRay Inc	Ben	Slotman
Navigate	Jacqueline	Cloos
LAVA Therapeutics	Henk	Verheul
Qurin Diagnostics	Geert	Kazemier

Stories behind some of these deals negotiated by business developers at IXA:

LAVA Therapeutics

In February 2017, VUmc licensed the Gamma-Delta T-cell engager platform technology to CCA spin-off LAVA therapeutics. It is a technology that activates the immune system to fight tumours. So far, the company has been quite successful in raising funds and milestone payments in partnerships in order to bring this technology forward. Our license agreement stipulates, among other things, that VUmc is entitled to an exit fee and royalties. With the IPO of LAVA in 2021, VUmc received shares and cash in exchange for previously contributed technology.

CimCure

In January 2017, the Booster technology developed at the lab of Arjan Griffioen was licensed to startup company CimCure. Since then, despite serious challenges among which the passing away of its CEO, the company managed to acquire significant funding in grants (€5M) and through investors (€5M) in order to prepare for clinical trials. In addition, Cimcure has several ongoing collaborations with reputable companies focusing on vaccines.

Qurin

In October 2017 and November 2020 VUmc licensed to startup company Qurin a technology that enables the early detection of cancers in urine. This non-invasive method was published in high-ranking journals by Renske Steenbergen and Jakko van den Nieuwenhuijzen. The technology can be applied on the nanofluidics platform developed by UTwente. Such that Qurin not only develops the biomarker panels established at VUmc, but also the nanofluidic technology, in order to have a robust solution for early cancer detection.

Awarded TKI public-private partnerships (internal Amsterdam UMC call):

Name main applicant	**Titel / Acronym**	**Call**
Sheila Krishnadath	Barrett's esophagus.	2017-2018
Louis Vermeulen	Long non-coding RNA Biomarker for	2018-2019
Michiel Pegtel	AQ-rate	2019-2020
Carlie de Vries	NR4 Ants	2019-2020
Eric Eldering	CLOSIT	2020-2021
René van Rijn	AMESMC	2020-2021
Renske Steenbergen	Med-aNaL	2020-2021
Dick Sterenborg	Ultra-Doc	2020-2021
Daniëlle Vugts	Cell-PET	2020-2021
Bart Westerman I	AI-IMPACT	2020-2021
Bart Westerman II	The Toxicity Atlas	2020-2021
Daniëlle Vugts	Click&Create	2021-2022

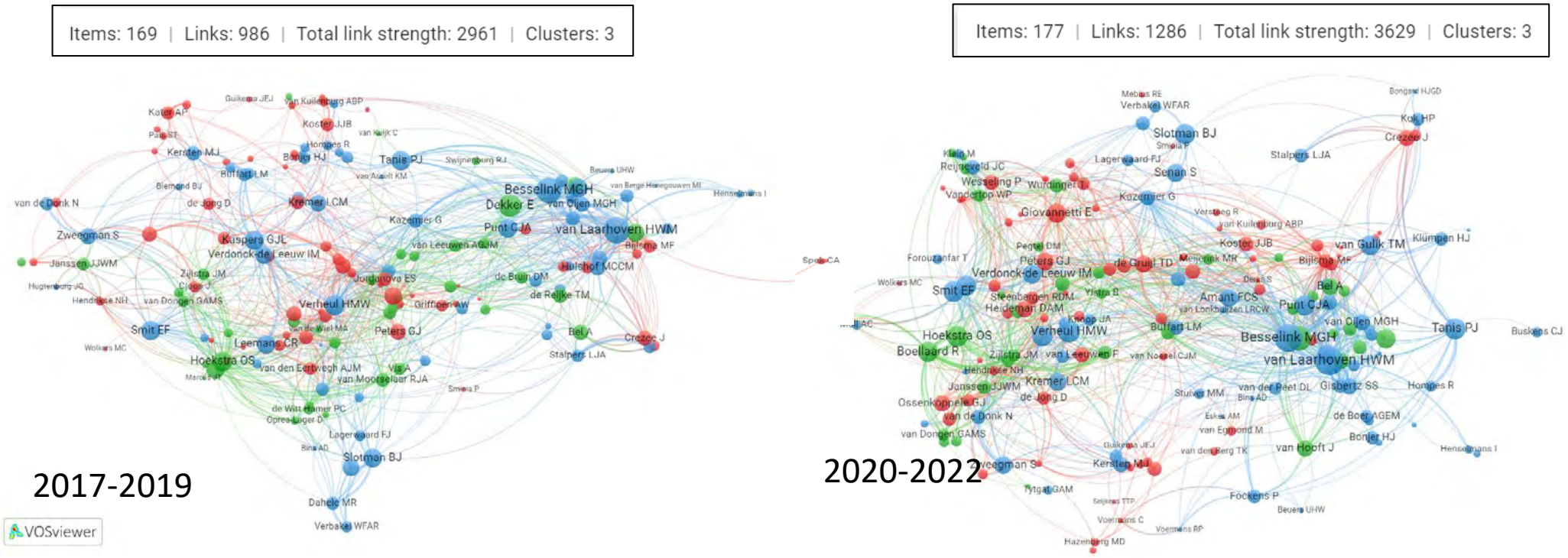
Research collaborations examples:

Within 6 months, a collaboration agreement was negotiated with a UK company during 2020 to further develop their diagnostic tool to detect opportunistic infections in fragile patients with hematologic malignancies. The PI asked for BD support as, at start, the company simply was looking to provide their tool and analysis capabilities without any further arrangement regarding intellectual property. Together with the PI, we successfully negotiated a fee to cover direct study costs and made favorable arrangements regarding IP. Currently, the project is mid-way and looking promising. In 2021, a collaborative research project using an innovative mouse model for osteosarcoma, developed at CCA, was referred to BD support at a late stage of the contracting. As the company provided their proprietary compounds, arrangements needed to be made to separate each parties' contributions to the project with respect to intellectual property. Within 3 months, we secured further academic use of the model and the results, and negotiated with the company a license fee in case the project results would lead to commercial benefits.

Collaboration opportunities examples:

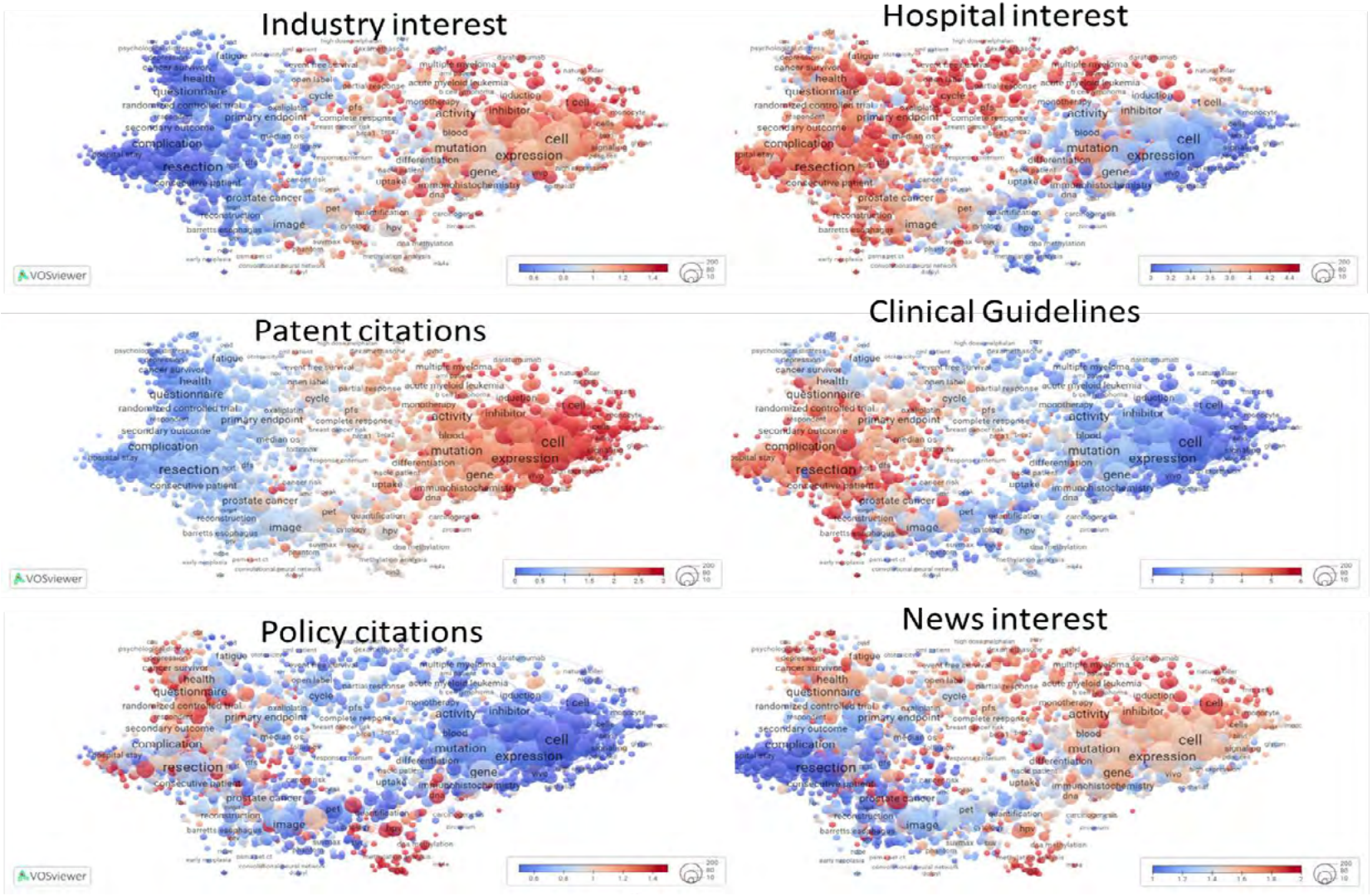
Over the last two years, Cancer Center Amsterdam expertise has been proactively presented to national and international companies by BD. We have visited 7 conferences and met with >70 biotech and pharmaceutical companies. We are currently discussing collaborative research projects with a number of these companies that would otherwise not have been attracted to CCA. An example is a European cell therapy company that now has 2 of our PI's advising them on their clinical trial set up . Both trials will run at Cancer Center Amsterdam, providing patients with new therapy options now, and hopefully also in the future.

Appendix 13: Cohesion between CCA PIs in publications



Publication interaction map for our Cancer Center Amsterdam PIs or the periods 2017-2019 and 2020-2022

Appendix 14: Interest based on keywords



Vos viewer
representation of analysis of the keywords Cancer Center Amsterdam publications in relation to the keywords that are of interest to or used in
a. Industry
b. Hospitals,
c. patent citations,
d. clinical guidelines,
e. policy citations,
f. News

Vos viewer analysis of the CCA publications based on keyword analysis used in the publications and their associated interest in the different domains analyzed. That is, when industry interest is analyzed the keywords of interest to industry are frequently used in the studies that show up red in the upper left figure.

These studies are mainly published by the cancer biology and immunology theme (CB&I publications are mainly found in this cloud, see figure 4). Hospital interest mainly lights up on the studies published in program 3 (upper right figure and figure 4)

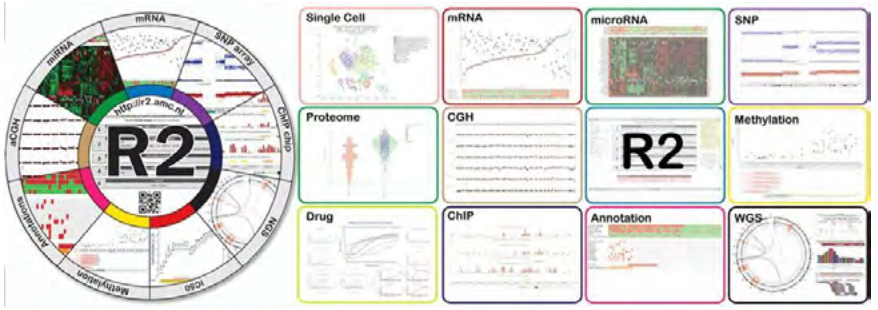
Appendix 15: Open science: R2 and Figlinq

Open Science Navigating a Sea of Data in a FAIR Ship

The world of biomedical research is confronted with a tsunami of data. How can we best explore and navigate this new wave?

With the advent of modern technologies and the increasing digitalization of scientific and medical instruments, oncology researchers are generating vast amounts of data at an unprecedented rate. This includes big data from fields such as genomics, transcriptomics, proteomics, epigenomics, as well as medical imaging analysis and precision radiotherapy, among others.
Embedded in Cancer Center Amsterdam's strategic vision, initiatives have been launched that open up our work to other researchers and societal stakeholders. These initiatives are rooted in open science following 'FAIR' principles and give researchers the tools to actively navigate big data and discover the next landmarks in cancer research and care.
In this section, we showcase two Cancer Center Amsterdam-supported initiatives that aim to empower both local and global cancer researchers and societal stakeholders with the ability to manage and analyze large datasets using user-friendly, yet state-of-the-art and powerful tools - *no computer coding or bio-informatic skills required*!

- **R2 Genomics Analysis and Visualization Platform**: A big data treasure trove for scientific discovery
- **Figlinq**: A whole new approach to the visualization, management, publication, and reuse of research data



R2 Genomics Analysis and Visualization Platform A big data treasure trove for scientific discovery

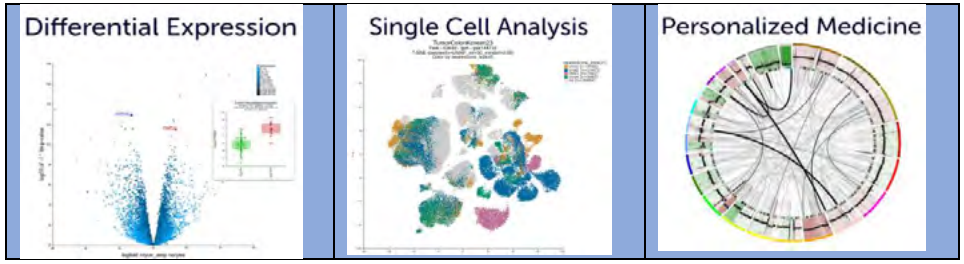
The in-house development of the R2 platform represents a significant contribution to multi-omics analyses in the field of oncology research. Strategic investments by Amsterdam UMC and Cancer Center Amsterdam have been pivotal to develop and realize the potential that big omics data sets offer.

The R2 Platform is an open, publicly accessible web-based genomics analysis *platform* designed to give biomedical researchers the ability to perform (complex) multi-omics analyses without the need for coding or bioinformatics expertise.

Researchers are now in the captain's seat with the power to hunt for buried treasures in datasets that are functionally associated with specific features of cancerous cells, like uncontrolled growth, metastatic capacity, drug resistance, or escape from immune surveillance.

The R2 platform hosts many publicly available genomic data resources that can be analyzed, explored, and visualized directly from the comfort of your browser, enabled by an extensive set of user-friendly interactive tools. In addition, the user can choose to work with their own data and relate their findings to other datasets, harnessing the power of thousands of measurements.

"Data and analyses can be shared between R2-users via the community options, making R2 an outstanding environment for discovery, hypothesis testing, and scientific collaboration." Dr. Jan Koster, Group Leader Cancer Bioinformatics & R2 Platform at Amsterdam UMC.



Examples of big data set analyses in the R2 platform. F.l.t.r.: Differential mRNA expression analysis between cell populations with and without N-Myc amplification. Gene expression networks based on single cell analysis in colon cancer. Integrative genomic analysis of mutations, translocations, duplications, and amplifications identified in a tumor from a single patient.

A comprehensive research environment

The versatile platform has been developed completely from within Amsterdam UMC by a team of bioinformaticians headed by Dr. Jan Koster, in close interaction with wet-lab scientists and clinical researchers. Since its inception in 2005, it has grown into a comprehensive research environment that answers real investigators' needs, with support from an in-house development team that is open to ideas, suggestions, and improvements.

Cancer Center Amsterdam strategic investment

In January 2022, Cancer Center Amsterdam made a strategic investment in R2 to support its continued development and improvements to empower researchers in gaining pivotal new insights from big data that could ultimately benefit patients with cancer (for an example, see Van Neerven et al. *Nature*).

This investment in R2 also represents Cancer Center Amsterdam's commitment to making research data "Findable, Accessible, Interoperable, and Reusable" (FAIR4). This is a set of principles that describe best practices for managing research data in a way that maximizes its potential for open science, reuse, and interoperability.

Milestones *since* January 2022:

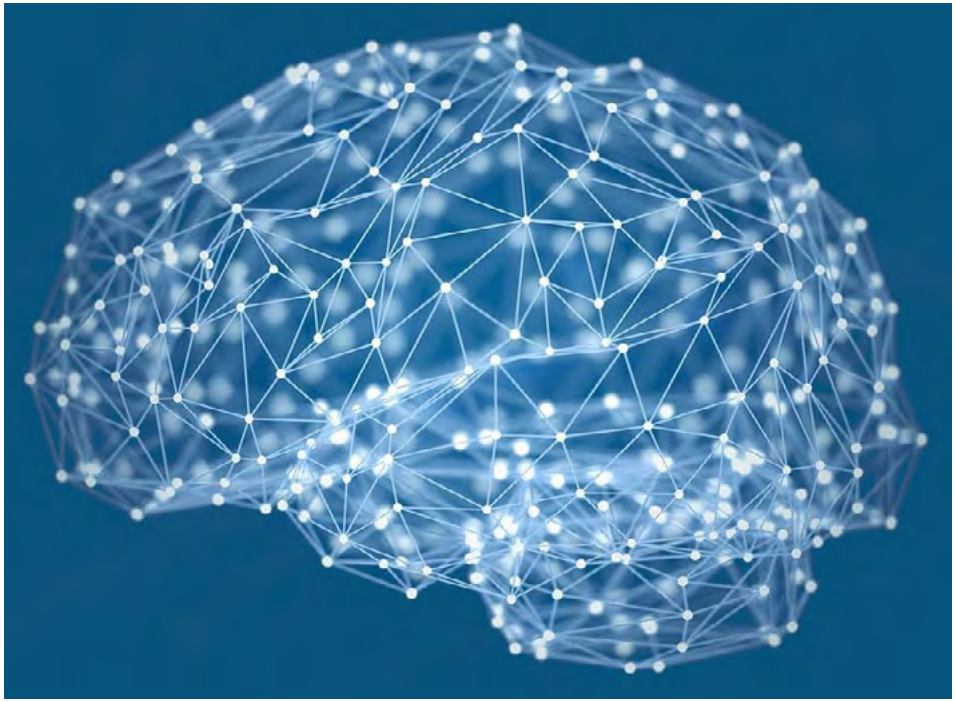
- Over 9,000 registered users
- ~3,800 datasets
- Included in 40+ grant applications
- 7 projects granted with small financial stake
- 2 projects granted with a large financial stake
- 3,106 new registered users
- Tens of thousands of unregistered users
  - 194,000 ip addresses served worldwide
  - >100,000 sessions/year
- 720 new user-requested platform resources
- New introduction workshop
- Updated tutorials book
- Active user support
- 2,328 citations in PubMed (May 2023)
- (Co-) authorships in 170 manuscripts
- Average impact factor of an R2 citation is 8.96
- Growth of the database to 3 million samples/cells

Future Horizons

With the CCA strategic investments and acquisition of funding through academic grants and partnerships, the R2 platform is set to continue to evolve by:

- Improving performance through upgrades in the source code
- Stimulating re-use of data sets by making these publicly available
- Enhancing capabilities in single cell analyses
- Further integrating multi-omics tools
- Investing in training and support for new and existing users.

"Recently, integrated analyses for personalized medicine, where copy number, mRNA expression, methylation and mutation data are combined into a comprehensive overview, aiding clinical decision making for a patient," says R2 founder Dr. Jan Koster. "As cohorts grow, they will undoubtedly form a treasure trove for scientific discovery."



Figlinq – A new, AI-driven, groundbreaking approach to the management, visualization, and reuse of research data

A collaborative platform for data analysis, interactive plotting, and publishing in data-connected smart manuscripts.

The sheer volume of data generated by bio-medical science today is challenging traditional methods of analysis and interpretation. Much data is never even published, leading to an estimated 80% of data that is irreversibly lost over 20 years – a catastrophic loss that exasperates the ongoing reliability and reproducibility crisis. In addition, the majority of published data are not findable, accessible, reusable or interoperable (FAIR). A whole new approach to data management is needed to improve data correlation and accelerate future discoveries.

Introducing Figlinq – a next-generation, no-code research data platform integrated with natural language models (GPT4).

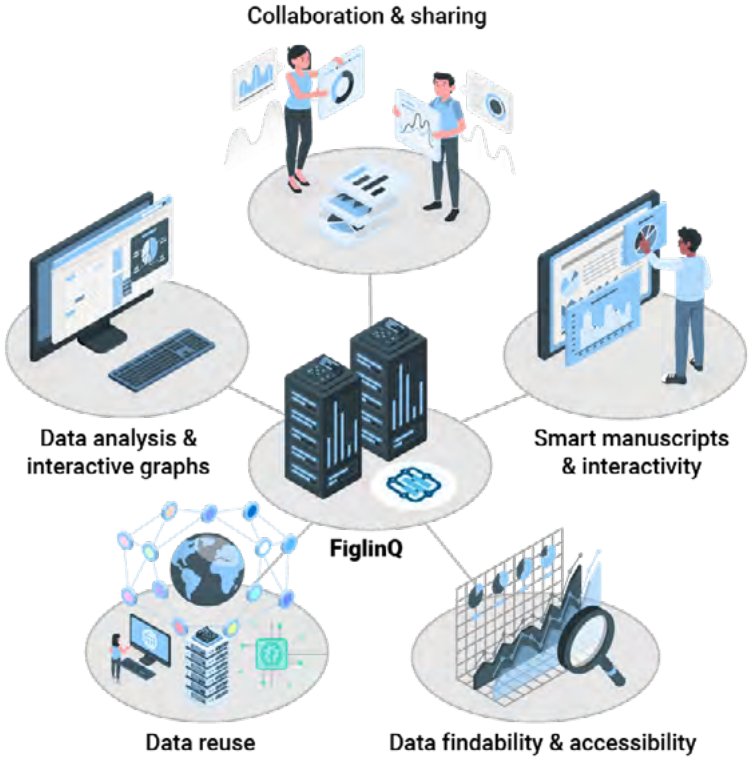
Figlinq (figlinq.com) is a collaborative, online environment for data workflows created by Cancer Center Amsterdam researcher Dr. Przemek Krawczyk. The platform can be used to create - and automatically and permanently connect - datasets with information-rich, interactive plots and figures, and to *publish entire data workflows* in smart, interactive manuscripts and reports, *without writing any code* (see a published example here).

In Figlinq, researchers can also manage, share, and reuse these workflows within their research groups or collaborations, as well as reuse public workflows of other researchers worldwide. Figlinq resembles an *electronic lab journal for data*, providing an integrated environment that potentially replaces multiple pieces of legacy offline software, *i.e.* Microsoft Office, Graphpad, Prism, SPSS Statistics, and Adobe Creative Suite.

"Following FAIR data principles, FigLinq is 'open science' at its core." Dr. Przemek Krawczyk, FigLinq founder and group leader at Amsterdam UMC.

Strategic Investment

The spin-off company Figlinq was co-founded with Amsterdam UMC through funding by an Innovation Exchange Amsterdam (IXA) Proof of Concept grant. In 2022, Figlinq received the prestigious Take-Off 2 grant from the Dutch Research Council (NWO). As of April 2023, the platform already had 300+ registered users from research groups in leading institutions across Europe, (Middle) East and the US. The platform is currently being evaluated for potential institution-wide roll-out within Amsterdam UMC.



Figlinq data management environment. Experimental data is recorded in Figlinq's smart data manager enabling in depth analyses, visualization, presentation, and open science.

For researchers	For Institutions	For publishers
Store, analyze and visualize data • Create interactive figures and figure collections • Collaborate during the entire research data lifecycle • Include entire data lifecycle in your manuscripts • Enable reuse of your data by others • Multiply impact of your research • Implement FAIR data practices	Reduce expenses on data software and hardware infrastructure • Facilitate data management for your employees • Make your organization and employees compliant with (FAIR) data stewardship policies • Improve your public image by promoting transparent, reproducible and open science	Embed interactive charts, figures and underlying data into your journals • Increase the impact of your publications • Improve and transparent review process • Align with current and future (FAIR) data stewardship policies • Improve your public image by promoting transparent, reproducible and open science

Figlinq, a leap in research data workflows. Figlinq brings essential data management, analysis, presentation, and publicizing tools together in a single integrated, domain-agnostic online application. This results in unprecedented transparency, open science, and data mining possibilities.

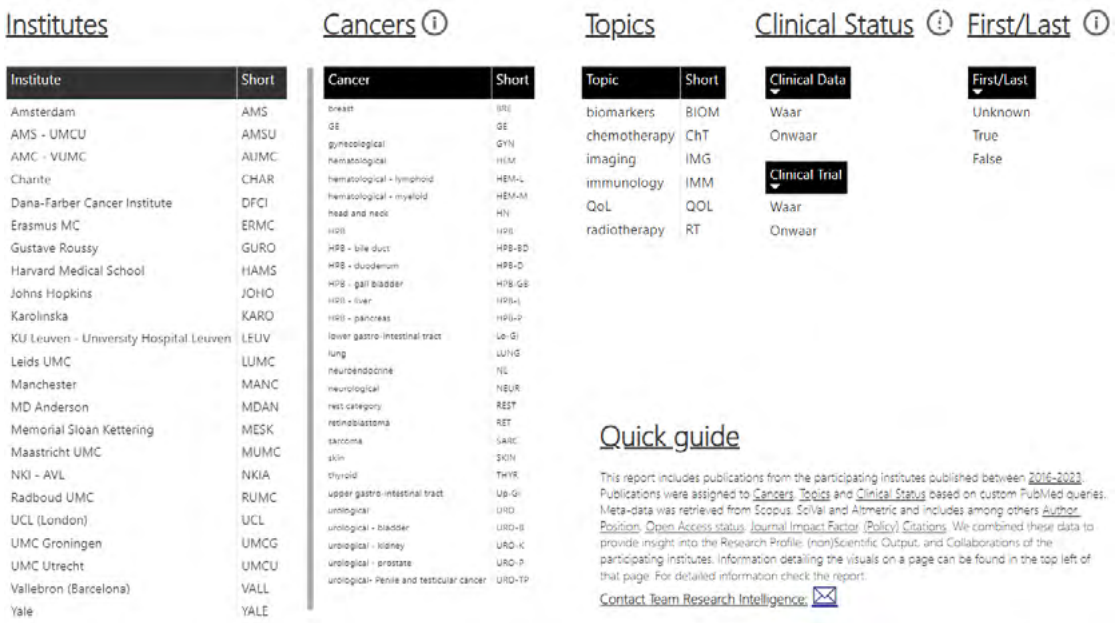
The future Is now: Figlinq with natural language model assistance

Figlinq has already been integrated with GPT4 natural language model, enabling *data visualization, analysis, and presentation using natural language*.

This is possible because Figlinq uses open and public data, visualization, and presentation formats that are already well understood by major large language models. Importantly, by end of 2023, Figlinq will also provide GPT4-driven *automated annotation of published data and metadata generation*, potentially enabling scalable reuse and mining of research data in a truly FAIR ecosystem.

"We will also focus on integration with other data collection and platforms to expand pooled data and expediate knowledge sharing. With enough scale, Figlinq will transition from a data visualization platform to a **data** platform that can connect data producers with other researchers and societal stakeholders," says Dr. Przemek Krawczyk.

Appendix 16: Research dashboard institutes



Institutes

Institute	Short
Amsterdam	AMS
AMS - UMCU	AMSU
AMC - VUMC	AUMC
Charite	CHAR
Dana-Farber Cancer Institute	DFCI
Erasmus MC	ERMC
Gustave Roussy	GURO
Harvard Medical School	HAMS
Johns Hopkins	JOHO
Karolinska	KARO
KU Leuven - University Hospital Leuven	LEUV
Leids UMC	LUMC
Manchester	MANC
MD Anderson	MDAN
Memorial Sloan Kettering	MESK
Maastricht UMC	MUMC
NKI - AVL	NKIA
Radboud UMC	RUMC
UCL (London)	UCL
UMC Groningen	UMCG
UMC Utrecht	UMCU
Vallebron (Barcelona)	VALL
Yale	YALE

Cancers

Cancer	Short
breast	BRE
GE	GE
gynecological	GYN
hematological	HEM
hematological - lymphoid	HEM-L
hematological - myeloid	HEM-M
head and neck	HN
HPB	HPB
HPB - bile duct	HPB-BD
HPB - duodenum	HPB-D
HPB - gall bladder	HPB-GB
HPB - liver	HPB-L
HPB - pancreas	HPB-P
lower gastro-intestinal tract	Lo-GI
lung	LUNG
neuroendocrine	NL
neurological	NEUR
rest category	REST
retinoblastoma	RET
sarcoma	SARC
skin	SKIN
thyroid	THYR
upper gastro-intestinal tract	Up-GI
urological	URO
urological - bladder	URO-B
urological - kidney	URO-K
urological - prostate	URO-P
urological- Penile and testicular cancer	URO-TP

Topics

Topic	Short
biomarkers	BIOM
chemotherapy	ChT
imaging	IMG
immunology	IMM
QoL	QOL
radiotherapy	RT

Clinical Status

Clinical Data
Waar
Onwaar

Clinical Trial
Waar
Onwaar

First/Last

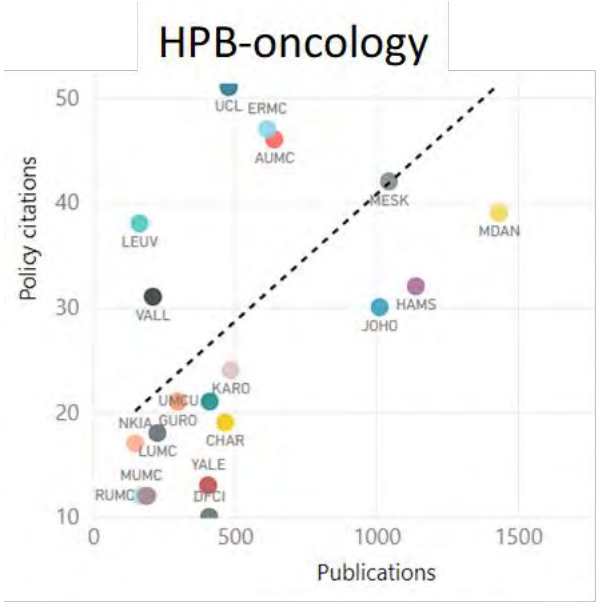
First/Last
Unknown
True
False

Quick guide

This report includes publications from the participating institutes published between 2016-2021. Publications were assigned to Cancers, Topics and Clinical Status based on custom PubMed queries. Meta-data was retrieved from Scopus, SciVal and Altmetric and includes among others Author Position, Open Access status, Journal Impact Factor, (Policy) Citations. We combined these data to provide insight into the Research Profile: (non)Scientific Output, and Collaborations of the participating institutes. Information detailing the visuals on a page can be found in the top left of that page. For detailed information check the report.

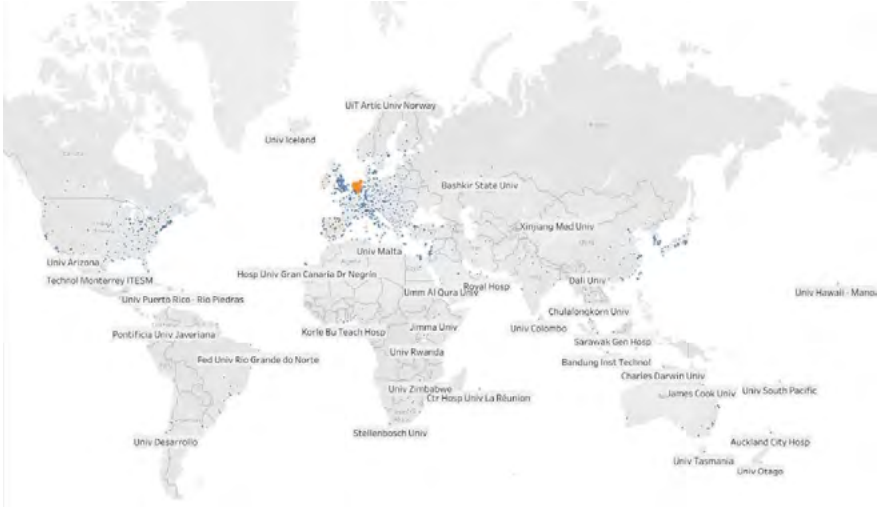
Contact Team Research Intelligence:

List of institutes, cancer types and subsets present in the research evaluation dashboard



Research dashboard analysis of Cancer Center Amsterdam HPB publications and their use in policy documents.

Appendix 17: World-wide collaborator map



Appendix 18: Use cases translation science

May 30, 2022

Winning combination of drugs for treating Chronic Lymphocytic Leukemia

Patients with Chronic Lymphocytic Leukemia (CLL) are better off with a combination of ibrutinib and venetoclax. These drugs each inhibit the growth of cancer cells in different ways. This is more effective than the standard treatment, a combined approach involving chemotherapy and antibody therapy, researchers of Amsterdam UMC discovered.

A scientific article was published today in The Lancet Oncology about this combination of the drugs ibrutinib and venetoclax against CLL. The NEJM Evidence also recently published on these findings.

CLL is a form of blood cancer that originates in the lymph nodes. It is the most common form of leukemia in the Western world, and no cure has been found for it yet. While treatments can keep the disease under control for many years, in time the drugs lose their effectiveness, because the cancer cells become resistant to them. This is why it is important to have access to several drugs, so that the patient can switch when necessary.

Much more effective

The arsenal of drugs for treating CLL has increased in recent years with the advent of inhibitors such as ibrutinib and venetoclax, which are given in the form of tablets. The combination of these two drugs has now been directly compared to the combination of standard chemotherapy and antibody therapy for the first time. The trial was conducted on 211 CLL patients, all older people who had never been treated before. The study, published in *NEJM Evidence*, reveals that a combination of the two inhibitors is much more effective than the standard approach.

> "By stopping for certain periods and taking the medication only when needed, you can use the drugs for much longer
>
> Arnon Kater
> Hematologist

Winning team

Years of fundamental research conducted at Amsterdam UMC helped set the stage for this clinical study. Molecular biologist Eric Eldering and hematologist Arnon Kater have been studying the behavior of CLL cancer cells in the lymph nodes and blood for more than fifteen years. Their research has produced valuable information about how cancer cells develop resistance to drugs.
Five years ago, professors Eldering and Kater found the first indications – initially in the laboratory, later in mice – that venetoclax and ibrutinib form an effective combination. Lab studies in cell cultures revealed what the 'winning team' of ibrutinib/venetoclax does: "Ibrutinib banishes malignant cells in the lymph nodes to the blood, where they are at their most vulnerable," explains Kater. "Venetoclax subsequently cleans them up."

Stopping and restarting treatment

A next question the researchers wanted to answer was whether you can safely stop the combination treatment after a year. "Ibrutinib is now given continuously until it no longer works," says Kater. "If you stop early, the disease quickly returns. But ideally, you want patients to be exposed to these drugs for as short a time as possible. There are several reasons for this. Ibrutinib has side effects such as diarrhea and joint pain. The drug also makes patients vulnerable to coronavirus infection and can damage the heart. It is also very expensive. Moreover, the shorter you take the drug, the less chance the disease will have to build resistance. By stopping for certain periods and taking the medication only when needed, you can use the drugs for much longer."

Arnon Kater, along with his Danish colleague Carsten Niemann, set up a study into whether patients could safely stop the combination of venetoclax and ibrutinib after one year. Using a highly sensitive test that can detect tiny amounts of cancer cells, they selected patients who had no detectable levels of CLL cells left. These patients were allowed to stop taking the medication. As soon the test revealed cancer cells again, the treatment was restarted. It was found that a significant number of patients were able to stop for longer periods of time. Moreover, the medication still proved to work if the disease returned. A study on this finding has now been published in *Lancet Oncology*.

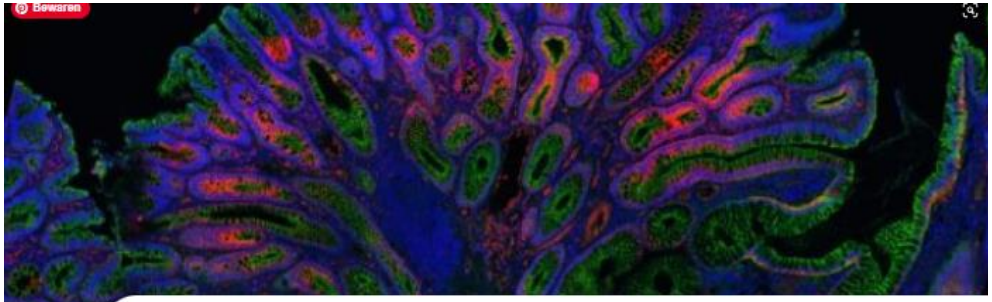
> We once proclaimed that CLL would one day change from a fatal disease to a chronic disease. We are on the right track to achieve this
>
> Eric Eldering
> Molecular biologist

CLL as a chronic disease

Is this good news for the patients? "We once proclaimed that CLL would one day change from a fatal disease to a chronic disease," says Eldering. "We are on the right track to achieve this. We can already treat patients for much longer before resistance develops." "That's because we have more drugs at our disposal," adds Kater. "But so far, with every drug we've trialed, we've seen it losing its effectiveness eventually. This is probably also true of this combination. You can safely stop and start again, but the question is how long you can continue to do this. We don't know that yet."

New studies

Eldering and Kater are therefore now investigating new ways to treat and hopefully cure this disease. In particular, studies of the metabolism of cancer cells on the one hand and of immune cells on the other appear promising. Last month the group published their findings in the scientific journals Blood and Blood advances respectively.



June 2, 2021

Outcompeting cancer: neutralizing the super-competitiveness of mutant intestinal stem cells

Intestinal stem cells are in a continuous competition with each other in what is normally a neutral process. But this balance can be disturbed if one stem cell acquires a mutation that gives it an unfair advantage. The disruption of the adenomatous polyposis coli (APC) gene turns intestinal stem cells into super-competitors and can lead to colon cancer.

Gene mutation gives advantage

Disruption of a particular gene in intestinal stem cells, called adenomatous polyposis coli (*APC*), leads to the formation of premalignant polyps, which is the earliest step in the development of colorectal cancer. Exactly how mutations in this gene initiate cancer is a subject of intense study. Stem cells with mutated *APC* have been shown to outcompete and replace their healthy counterparts, but the mechanisms underlying this competitive advantage were unclear. A new study published in *Nature* from the lab of Louis Vermeulen, Principal Investigator at the Center for Experimental Molecular Medicine at Amsterdam UMC and the Oncode Institute, sheds light on why *APC*-mutant stem cells have the upper hand.

'Super-competitors'

The team showed that *APC*-mutant stem cells send signals to neighboring healthy stem cells that instructed them to differentiate, rather than self-renew. By actively forcing healthy stem cells out of the crypt bottom, the mutant stem cells could quickly overtake the vacant positions within the crypt, a mechanism referred to as super-competition. "Intestinal stem cells are in a continuous competition with each other in the crypt," says first author, Sanne van Neerven.

> "Normally, this is a neutral process. But it can be disturbed if one stem cell acquires a mutation that gives it an unfair advantage."

The thin, protective layer of cells lining the intestines is one of the most rapidly renewing tissues in the body, and for a good reason. The mission of these cells is to absorb water and nutrients from the gut, a hostile environment that quickly damages cells. Resident stem cell populations deep within the tiny undulated folds of the epithelial lining, called intestinal crypts, are responsible for generating new cells to replace those that are continuously lost. These intestinal stem cells can both self-replicate, producing more stem cells, or differentiate, becoming a variety of specialized cell types for different functions: a tightly controlled balancing act.

APC-mutant kryptonite

Importantly, the team discovered a way to interfere with the signals sent by *APC*-mutant stem cells. Lithium shifted the competitive benefit towards the healthy stem cells, and prevented *APC*-driven adenoma formation. "We revealed that boosting healthy intestinal stem cell fitness by using lithium, which activates the Wnt pathway, could revert this unfair competition and prevent the formation of adenomas," says Sanne.

A prevention strategy

Mutations in the *APC* gene are one of the most common and earliest events that lead to the development of colorectal cancer. Inhibition of *APC*-driven super-competition could therefore be a powerful tool to prevent the initiation of intestinal cancer. This is especially relevant for patients with familial adenomatous polyposis (FAP), a disorder caused by a hereditary defect in the APC gene. FAP patients develop multiple adenomas in their intestine starting at an early age and are predisposed to the development of colorectal cancer. Treatment of these patients with lithium may block *APC*-mutant stem cells in the intestine and prevent colon cancer initiation and progression. As a medicine, lithium has been used to treat patients with bipolar disorder for decades. Prof. Louis Vermeulen: "We discovered that a similar set of Wnt inhibitors is expressed by FAP adenomas and therefore we propose the use of lithium as a chemoprevention strategy for FAP patients. We have recently acquired a grant from the Dutch Cancer Society (KWF) to perform a clinical trial studying this potential preventive strategy."

Appendix 19: Diamond program

December 7, 2022

Education / Shine like a Diamond

In 2014, the Oncology Graduate School Amsterdam (OOA) launched the 'Diamond Program', an innovative program to support highly talented Master students in pursuing a doctorate degree. The premise of this NWO-funded program (€ 800 000) was based on the American graduate school model in which PhD candidates freely choose which group and research suits them best, rather than applying for an advertised PhD position.

From 31 applications to the program, eight qualified students in the final stages of their MSc programs were offered the opportunity to meet principal investigators (PIs) affiliated with Cancer Center Amsterdam or Netherlands Cancer Institute during a 'speed-dating' style event. Next, the students chose three labs to perform rotations – similar to the graduate school system in the USA but with a duration of two weeks per rotation.

In the final stage of the selection process, research proposals were drafted by the students in collaboration with their selected PIs. Dr. Esther Ruhé, project manager of the Diamond Program: "The students essentially wrote their own PhD research projects while attending the OOA grant-writing workshop. Based on evaluation of these proposals by an external

Making excellence shine

"It has been an incredible journey," Esther says. "The four Diamond PhD candidates surpassed all expectations, by far."

The output?

- 43 peer reviewed publications, including original scientific articles in high-profile journals such as *Nature* and *Blood*, and reviews in *Nature Reviews Molecular Cell Biology* and *Cell Stem Cell*
- Several editorial comments highlighting the importance of these cancer research findings
- Four PhD theses, of which one with the distinction *cum laude*
- Selected and invited to international conferences
- Prestigious international awards
- A wealth of new international collaborations to fuel even more discoveries

> "Initially, I was skeptical whether MSc students would have sufficient insights to write their own PhD trajectories, but - with support from their PIs - all succeeded in crafting high-quality proposals.
>
> Prof. Hein te Riele,
> Member Executive Board - Oncology Graduate School Amsterdam.

"All of this is evidence that the Diamond Program really proved its value and also jumpstarted the careers of the PhD candidates," says Esther. "All our Diamond students have successfully continued their careers with positions in cancer research or medicine."

> "The Diamond Program succeeded in attracting top research talents and provided optimal conditions for these gifted students to reach their true potential.
>
> Dr. Marcel Spaargaren,
> Member Executive Board – Oncology Graduate School Amsterdam.

the last Diamond student. Unfortunately, the necessary funds to continue the program have not been acquired.

Esther: "Together, we are working to secure funding in collaboration with Cancer Center Amsterdam and the Netherlands Cancer Institute. I am hopeful we can continue this education program to select top talents and have them shine in cancer research."

For more information about Oncology Graduate School Amsterdam, the Diamond Program, or opportunities to sponsor continuance of this program, contact Dr. Esther Ruhé.

Meet the Diamond Program PhD students:

> If you have the ambition to become an independent and highly impactful researcher, the Diamond Program is the best thing that can happen to you.

Inge van der Werf
Diamond Program PhD Student, PI Prof. Jacqueline Cloos, Department of Hematology, Cancer Center Amsterdam.

Inge's research focused on mRNA splicing in pediatric and adult acute myeloid leukemia (AML) as a therapeutic target. In pursuit of technical know-how and answers to her research questions, she visited the labs of Prof. Catriona Jamieson at the University of California (San Diego) and Dr. Ruben van Boxtel at the Princess Máxima Center for Pediatric Oncology and Oncode Institute. Based on her work during the Diamond Program, Inge and her scientific collaborators have published 8 peer reviewed articles, including a first author publication in the prestigious journal *Cell Stem Cell*. She is currently a postdoc in the Van Boxtel lab.

> The freedom to choose what and where you want to study is one of the things that makes the Diamond Program unique. I am incredibly grateful to have been given this opportunity.

Josephine Kahn
Diamond Program PhD Student. PIs Prof. René Bernards, Molecular Carcinogenesis, Netherlands Cancer Institute, Prof. Benjamin Ebert, Hematology, Dana Farber Cancer Center.

The Diamond Program enabled Josephine to pursue her interest in chemotherapy-resistant leukemia. Working in the Ebert lab (Dana Farber Cancer Institute - Boston) and the Bernards lab (NKI), she discovered that mutations in the *PPM1D* gene drive the growth of malignant cells in the presence of chemotherapy and that these cancer cells can be killed using a PPM1D inhibitor. Josephine's work during the Diamond Program resulted in 4 peer reviewed publications including two in the prestigious journal *Blood* (one of which was selected as one of the top 10 papers of the year by the journal). She is currently a Clinical Fellow in Medicine at Harvard Medical School.

> *I am forever grateful for the opportunity to participate in the Diamond Program and hope that future PhD students will have the opportunity to benefit from this amazing initiative.*

Sanne van Neerven
Diamond Program PhD student. PI Prof. Louis Vermeulen, Center for Experimental Molecular Medicine, Cancer Center Amsterdam.

In the Vermeulen lab, Sanne studied tissue renewal and carcinogenesis in the intestine. One of her key interests was in competition between cells and the link to cancer. She established that mutations in intestinal stem cells can confer a competitive advantage through a novel mechanism called 'super competition' and that this provides a basis for the development of colorectal cancer. For this discovery, Sanne won the prestigious international Birnstiel Award and the UNESCO/L'Oreal women in science rising talent award. Sanne is an author on 22 scientific publications, including first author publications in the top scientific journals *Nature* and *Nature Reviews Molecular Cell Biology*. After the Diamond Program, she is continuing her career in cancer research as a postdoc at the University of Cambridge (UK).

> I cannot stress enough how valuable this experience has been for me.

Kevin Kos
Diamond Program PhD student. PI Prof. Karin de Visser, Tumor Biology & Immunology, Netherlands Cancer Institute.

Kevin's research focus has been on the role of immunosuppression in metastatic breast cancer. Kevin established that CD4+ regulatory T cells (Tregs) cells facilitate the metastasis of cancer cells into lymph nodes. Kevin is an author on 10 scientific articles including first author publications in the respected journals *Cell Reports* and *Annual Reviews Cancer Biology*. He will defend his PhD thesis in January 2023 and has started a position as Program Coordinator Immunotherapy at the Dutch Cancer Society (KWF).

Appendix 20: Use cases program 1

Use case Cancer Biology: New genes in DNA repair

July 7, 2021

Discovery of New Genes in DNA Damage Repair by CRISPR Screening Technology at Amsterdam UMC

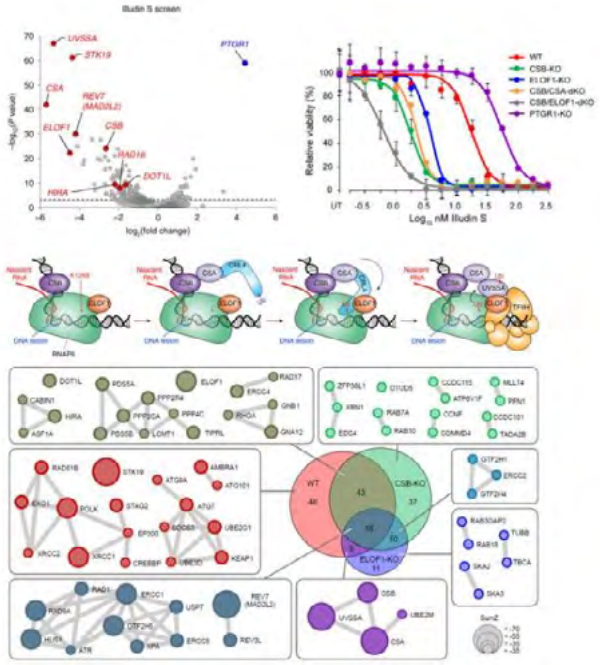
With help of their colleagues, researchers Klaas de Lint and Rob Wolthuis (Cancer Center Amsterdam and Department of Human Genetics) introduced a full-genome CRISPR functional genetic screening pipeline in Cas9-inducible diploid cells to identify genes involved in DNA damage responses. In collaboration with the Martijn Luijsterburg lab (LUMC) they first focused on identifying the human genes involved in the process of Transcription Coupled DNA Repair. Their discoveries were published in Nature Cell Biology this month.

With the Nobel prize-winning application of CRISPR technology in human cells, it recently became possible for researchers to systematically knock-out human genes in lab-grown cells to reveal their roles in cancer relevant biological processes.

The Wolthuis lab (Oncogenetics, Department of Human Genetics) at the Cancer Center Amsterdam, implemented a new pipeline for so-called pooled lentiviral full-genome CRISPR-Cas9 knockout screening. A collection of 71,000 different CRISPR-lentiviruses was used to create a population of millions of cells, each containing a knockout of a unique human gene. Subsequently it was measured which genes are essential for cell growth and survival, before or after treatment with a specific DNA-damaging drug. Thereby the researchers were able to pinpoint the human genes and pathways involved in the underlying DNA repair pathway of this study, called Transcription-Coupled DNA Repair (TCR).

Apart from all the known TCR genes, the previously uncharacterized *ELOF1* gene was identified as a top hit. Next, a wide range of experimental approaches was used, including follow-up drug screens in isogenic cell lines, to elucidate the precise function of ELOF1. The researchers discovered that ELOF1 is a novel component of the mRNA synthesis machinery (called the RNA-polymerase II complex) but also acts as an important factor in DNA repair, when the RNA-polymerase II complex encounters a transcription-blocking lesion.

ELOF1 is particularly important to help cells deal with UV and chemotherapeutic compounds, but also plays a role in controlled cell division. These findings helps in the understanding of hereditary cancer syndromes which are linked to DNA damage repair genes, as well as the effects of targeted drugs used in cancer therapy.



Use case Cancer Immunology: A New AML Vaccine Takes the Mainstage

At the 2022 meeting of the American Society of Hematology, Prof. Arjan van de Loosdrecht was invited to present the ADVANCE II study, a phase II clinical trial testing a new vaccine to treat residual disease in patients with acute myeloid leukemia.

From an original idea born of fundamental research, followed by preclinical validation and vaccine development, to treating patients in a clinical trial: ADVANCE II is a prime example of Cancer Center Amsterdam's 'from-bench-to-bedside' philosophy to offer new possibilities to patients with cancer.

Acute Myeloid Leukemia What is it?

Leukemia is a general term for cancers originating in the blood cells. Acute myeloid leukemia (AML) is a fast-growing cancer in which too many **abnormal immature white blood cells** (myeloblasts or blasts) multiply uncontrollably, filling up the bone marrow and preventing production of other cells important for survival, namely red blood cells and platelets. This leads to anemia, infections, and abnormal bleeding. The outlook for AML patients is bleak: 5-year overall survival rates are only 5–15% in older patients (>65 years), and 30% in younger patients.

At the lab bench: basic cancer-immunology research delivers a clinical concept

"The ADVANCE II clinical trial is a culmination of the work of many researchers and clinicians," says Prof. Arjan van de Loosdrecht. "The initial basic research was performed almost 20 years ago in our Hematology Laboratory together with principal investigators Tanja de Gruijl and Gert Ossenkoppele. We were able to isolate immature abnormal white blood cells from patients – called blasts - and turn these into *leukemic dendritic cells* in the lab."

Dendritic cells are key immune players that can activate and prime other immune effector cells, like T and B lymphocytes, to recognize and fight tumor cells. Dendritic cells that are derived from immature leukemia cells have unique potency because they come pre-loaded with multiple *acute myeloid leukemia* specific antigens.

"In preclinical models, we showed that these dendritic cells derived from immature leukemia cells significantly boosted the immune reaction against cancer. Then we discovered that we could create similar cells from an AML cell line which can be propagated indefinitely. This was truly exciting. It opened the door to a potential 'off-the-shelf' effective AML vaccination strategy, avoiding the laborious and costly personalized vaccine approach."

Dendritic cells The "traffic cops" of the immune system

Dendritic cells (DC) are key regulators of the immune response. They reside in peripheral tissues and are constantly sampling their environment for foreign antigens – any substance that your immune system does not recognize. If they detect something suspicious – like a virus – dendritic cells call for help and direct the flow of responding immune cells to investigate the threat.

The DC cops also have the unique ability to capture suspected antigens and transport the potential perps to processing centers in the lymph nodes. Here, detainees are presented to other immune cells (B cells) that produce antibodies specific to the antigen - they can fit onto the offending antigen like a key to a lock. Once antibodies are released into the body, they hunt for and lock onto their target antigens (and anything associated with that antigen, like a bacteria or virus particle or cancer cell), and blow the whistle for the immune system to destroy the whole target.

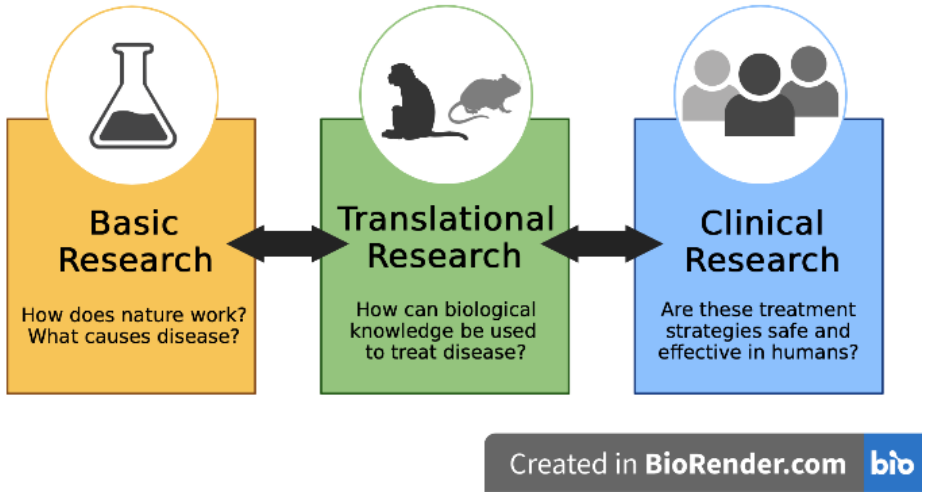
"This was truly exciting. It opened the door to a potential 'off-the-shelf' effective AML vaccination strategy." - Prof. Arjan van de Loosdrecht

Into the clinic: Phase 1 and spin-off

"In a Phase 1 study of a novel medicine, you are asking: is this medicine basically safe to give to patients?" says Arjan.

Twelve elderly acute myeloid leukemia (AML) patients that were at high risk of relapse and ineligible for other treatment were enrolled in the study. "We found that the DCP001 vaccine was safe and well tolerated," says Arjan. "We also noted there was a clearcut distinction between patients with or without circulating leukemic blasts. Patients with no circulating blasts showed an unusually prolonged survival - on average 36 months from the start of vaccination, whereas patients with circulating blasts died within 6 months. Patients who survived long term also showed signs of immune stimulation." Although the study size was too small to draw definitive conclusions, "I said to my colleagues: guys, this could be

real." It was time to take the promising dendritic cell-based immunotherapy to the next level.



Clinical phase 2: Does the treatment really work?

"A phase two study asks the question: how *effective* is the vaccine? Does it really work?" says Arjan. To launch a phase 2, the team needed more money. "Plus, we also had to continue the fundamental research and optimize assays to see – among other things – what effect the vaccine was having on the immune system."
Together with colleagues and corporate partners, Arjan formed a consortium with partners in Germany, Norway, and Sweden which successfully secured a € 6 million grant from the EU Horizon 2020 program.

A new horizon

Despite challenges presented by the COVID-19 pandemic, the Phase 2 study – termed the ADVANCE II trial – successfully enrolled 20 patients who were in their first complete remission (CR1) due to standard treatment, but still had the presence of cancerous cells that resisted treatment.

Vaccine DCP-001 How does it work?
Abnormal immature white blood cells were isolated from an AML patient's blood and cultured in the lab along with growth factors that stimulated the immature cells to *differentiate* into **dendritic cells** by triggering a series of genetic and biochemical changes. The AML cell line DC1 can be propagated indefinitely and are intrinsically covered/equipped with leukemia-specific antigens capable of stimulating a strong immune response against the cancer cells. They also produce a variety of cytokines and chemokines that help to attract and activate immune cells.

Administration of the vaccine: The mature dendritic cells inactivated by high-dose irradiation are administered to the patient as a vaccine via skin injection.
The data from the trial showed the vaccine had the potential to significantly improve survival for AML patients. Prof. van de Loosdrecht was excited to present the results of the completed ADVANCE II trial at the 64th American Society of Hematology Annual Meeting (ASH) in December 2022 in New Orleans, US.
"We saw substantial responses in five patients who went from detectable to undetectable disease status. Two additional patients had at least a tenfold reduction in leukemic blasts, and seven remained stable. Six had a relapse within 32 weeks of vaccination," says Arjan.
These results indicate a clear improvement compared to current standard of care. The long-term benefits are still not clear; at the time of the meeting, median relapse-free survival was not yet reached, with 12 out of 20 patients still in complete remission (ranging from 16 to 47 months after start of treatment).
The observed immune responses were in line with the improved clinical observations. In 17 of 20 patients (85%), DCP001 vaccination induced a durable immune response.

Looking ahead

The promising DCP001 cancer vaccine is a result of concerted efforts by Cancer Center Amsterdam researchers to translate fundamental biologic insights gained from research (bench) to meaningful clinical applications (bedside). To bring this new immunotherapy to more AML patients in need, the company Mendus has come aboard to tackle clinical-grade production requirements and regulatory hurdles on the way towards market approval.
Arjan points out: "At this time, it's important to note that this is still in an early-stage, and more research is needed to determine the vaccine's safety and efficacy. Looking ahead, we are working very hard to initiate new trials aiming to combine the DCP001 vaccine with other drugs to improve outcome for even more AML patients. We also really want to explore a maintenance program, where vaccination can be adjusted based on residual disease monitoring. Looking even further, we would like to see if the vaccine can be used after stem cell transplantations in AML patients to reduce the risk of recurrence in younger patients. There are many directions to pursue – and of course, all new studies need funding – but these are the next horizons."

"I hope that in 6-7 years, I will see a trial where we can intervene at a very early stage with our therapeutic vaccine, and are able to derail acute disease. That is a dream I want to see a reality, yes, what a difference that would make for patients."

Appendix 21: Use case program 2

Use case GBM monitoring using liquid biopsies

Can liquid biopsies be used to monitor progression of disease in patients with brain cancer?

Liquid biopsies have been heralded as a potential game changer in cancer detection and management. The analysis of blood, saliva, or urine for traces of cancer offers a non-invasive and sensitive method for diagnostics and monitoring of treatment response. Cancer Center Amsterdam is pioneering the use of liquid biopsies for cancer research and implementation in clinical care. Through the establishment of a Liquid Biopsy core facility, funded by the CCA Foundation many innovative research projects have been initiated. Here, we highlight the efforts of the Neuro-oncology Research Group to develop a test for monitoring therapy response and disease progression in glioblastoma patient based on liquid biopsies.

Blood of cancer patients is a rich source of cancer-related biomarkers such as tumor educated platelets (TEPs), circulating tumor cells (CTCs), cell-free circulating tumor DNA (cfDNA), and extracellular vesicles (EVs).

Dr. David Noske, a neurosurgeon and director of the Neuro-oncology Research Group (NRG), and colleagues Prof Tom Würdinger. Dr. Myron Best and Dr. Nik Sol have teamed up with the Liquid Biopsy Center (LBC) at Amsterdam UMC - Cancer Center Amsterdam to develop innovative solutions to identify and differentiate glioblastoma progression in patients, an unsolved daily clinical problem. Glioblastoma is a highly aggressive form of brain cancer with a poor prognosis. During the course of the disease, up to 66% of patients experience contrast-enhancing lesions on an MRI scan that resolves spontaneously over time without additional treatment. These lesions result from therapy-induced radio necrosis, a phenomenon also known as glioma pseudo-progression. The challenge lies in accurately determining real tumor progression versus treatment-related effects, as pseudo-progression or radio necrosis

Dr Noske and his team were involved in the development of ThromboSeq, a technique that established that pieces of cells found in the blood contain information that can be used to support clinical decision making for glioblastoma patients. They are currently working to bring this test into the clinic.

Tumor-educated platelets: a 'quantitative fingerprint'

Blood platelets are cell fragments in the blood that are implicated in blood clothing and initiation of wound healing. Although platelets do not contain a nucleus, they possess RNA and the machinery to splice and express thousands of mRNAs.

The team of Noske and Würdinger discovered that platelets isolated from cancer patients have a distinct pattern of tumor-associated RNA molecules. The group coined the term 'tumor-educated-platelets' (TEPs) to refer to platelets that have been exposed to tumor cells or tumor-related factors. This important discovery opened the door to using platelets as a biomarker for the detection of cancer.

The NGR team then developed advanced sequencing techniques and AI-assisted analysis and was able to deduce glioblastoma classification scores – 'quantitative fingerprints' – that accurately reflected the real-time status of glioblastoma tumor cells during therapy follow-up.

The research team created two parallel approaches for glioblastoma monitoring. The TEP-Glioblastoma-Score reflects tumor burden and can indicate potential tumor regression following resection. Additionally, an algorithm has been developed to discriminate between actual tumor progression from pseudo-

progression. Preliminary results yielded a correct diagnosis of tumor status 85% of the time.

Towards Clinical Implementation

For validation of the diagnostic assay, the group plans to collect longitudinal blood samples from glioblastoma patients in the Netherlands and the United Kingdom. The samples will be obtained at various stages of treatment and disease progression. The aim is to optimize the TEP-Glioblastoma-Score and the progressor versus non-progressor test, aiming for a target accuracy rate of over 95%. Successful validation of the test is expected to bring liquid biopsy monitoring of glioblastoma patients one step closer to clinical implementation. Funding for the TEP project and a promising complementary method in development at Cancer Center Amsterdam based on cell-free DNA was provided by KWF.

The Liquid Biopsy Center: strategic choices and achievements

Established in 2017 with substantial funding from the Cancer Center Amsterdam Foundation, the LBC serves as a central facility within Cancer Center Amsterdam. It coordinates liquid biopsy-related cancer research projects initiated by Cancer Center Amsterdam researchers, in collaboration with clinical departments, the clinical chemistry department, and the central biobank facility. The LBC offers hands-on support for biobank projects, ensuring legal-ethical compliance, standardized processing, and storage protocols for high-quality biofluidic samples. Noteworthy achievements of the LBC include its unique centralized setup, collaborations with multiple clinical departments and hospitals, extensive sample collection, and the publication of research projects utilizing LBC samples. **The Liquid Biopsy Center is currently expanding its network of participating regional hospitals** (see Collaborative Regional Care and Research Network in Oncology) **to grow this crucial resource to empower novel discoveries in oncology research and care.**

Liquid Biopsy Center CCA

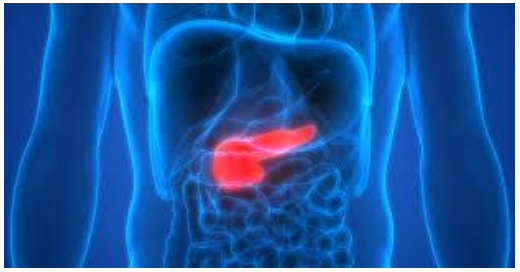
At a glance

- 17 biobank projects initiated
- 8,008 samples collected from 4,055 patients
- 46 sample requests
- 1,599 issued samples

Strengths

- Comparable high quality samples due to centralized logistics
- Unique in its central and hands-on setup within The Netherlands
- Networking with local hospitals being established
- Automated clinical annotations from the electronic health record in development
- Active spouse program for the collection of age- and lifestyle matched control samples

Appendix 22: Use cases program 3



Use case pancreatic cancer

Realizing progress through the forging of national alliances

Pancreatic cancer is one of the deadliest forms of cancer, with a low survival rate and significant impact on quality of life. Historically, the 5-year survival probability is only 9% and more than 2800 Dutch patients die due to this illness each year. Only through collaboration and cooperation can we realize progress against this disease and improve care for patients with pancreatic tumors. Cancer Center Amsterdam has been a leader in forging national alliances that have made real progress towards this goal.

Multiple national collaborative initiatives have been initiated in the Netherlands to push the boundaries of patient care in pancreatic cancer. At Cancer Center Amsterdam (CCA), our researchers are actively involved in these initiatives, playing crucial roles by leading, collaborating, sharing knowledge, and achieving innovation in the field.

Cancer Center Amsterdam Professors Marc Besselink (surgeon), Olivier Busch (surgeon), Hanneke van Laarhoven (medical oncologist), Geertjan van Tienhoven (radiotherapist) and Hanneke Wilmink (medical oncologist) have central roles in executive boards or steering committees of the DPCG.

"For more than a decade, we have been laying the groundwork and partnered with patients to advance clinical research and drive greatly needed innovation. The results of clinical trials, like PREOPANC, clearly show our collaborative forces are making an impact for patients with pancreatic cancer." Prof. Marc Besselink, Professor of Pancreatic and Hepatobiliary Surgery at Amsterdam UMC – Cancer Center Amsterdam.

Collaborations: Push for progress in pancreatic cancer care

- **The Dutch Pancreatic Cancer Group (DCPG)**

Formed in 2011, the DPCG is a multidisciplinary collaboration that brings various national experts together, including surgeons, oncologists, radiologists, pathologists, and scientists. The aim is to improve the management and outcomes of patients with pancreatic cancer through research and implementing evidence-based practices.

- **The Dutch Pancreatic Cancer Project (PACAP)**

In the Netherlands, PACAP - initiated by DPCG - is the leading platform for long-term research on the treatment and patient-reported outcomes of pancreatic cancer. To facilitate scientific research, PACAP provides the infrastructure and quality guidelines for collecting clinical data, patient-reported outcomes, and biobanking of blood and tumor tissue.

- **Delta Plan Pancreatic Cancer**

Inspired by the name of the revolutionary water defense system in the Southwest of the Netherlands, 'Deltaplan Alvleesklierkanker' is a collaboration between the DCPG and patient organizations in the Netherlands (Maag Lever Darm Stichting and Living With Hope) that focuses on personalized treatment strategies based on molecular profiling.

DPCG
Dutch Pancreatic Cancer Group

Clinical Trials: Significantly improved long-term survival with preoperative chemoradiation for pancreatic cancer patients

The PREOPANC trial - coordinated by researcher Eva Versteijne, a Radiology Oncologists at Cancer Center Amsterdam - evaluated the effectiveness of preoperative chemotherapy and radiation therapy in patients with resectable and borderline resectable pancreatic cancer. The trial demonstrated improved overall survival and tumor downstaging in patients who received neoadjuvant

treatment before surgery. These findings have led to changes in guidelines, with the inclusion of neoadjuvant therapy as a standard treatment option for selected patients.

"The outcome of the PREOPANC trial revealed an improved five-year survival from 6.5% to 20.5 % by administering chemotherapy and radiation before the operation. Until now, pancreatic cancer has shown extreme resilience to treatment. As such, a threefold increase in survival rate is a truly major advancement." Dr. Geertjan van Tienhoven, radiation oncologist at Amsterdam UMC – Cancer Center Amsterdam.

PREOPANC Trial: The PREOPANC trial evaluated the effectiveness of preoperative chemotherapy and radiation therapy in patients with resectable and borderline resectable pancreatic cancer.

ESPAC-4 Trial: The ESPAC-4 trial investigated adjuvant chemotherapy options for patients with resected pancreatic cancer. The trial compared gemcitabine alone with a combination of gemcitabine and capecitabine.

PRODIGE 24/CCTG PA.6 Trial: This trial evaluated the role of a modified chemotherapy regimen in patients with metastatic pancreatic cancer.

DPCA-01 Trial: The DPCG initiated the DPCA-01 trial, which investigated the role of circulating tumor DNA (ctDNA) in predicting treatment response and monitoring disease progression in patients with pancreatic cancer.

Global recognition

The DPCG, along with Cancer Center Amsterdam and other prominent hospitals and research centers in the Netherlands, is actively involved in conducting clinical trials, advancing personalized medicine approaches, and participating in international collaborations (see text box). Their contributions to research and the development of treatment guidelines have gained global recognition.

Surgeons at Cancer Center Amsterdam run the European training program in robot-assisted pancreatic surgery

Robot-assisted minimally invasive pancreatic surgery is the latest advancement for patients with pancreatic cancer that are eligible for tumor resection. This innovative method aims to reduce complications, blood loss, pain, and improve recovery times.

With the help of funding from the Cancer Center Amsterdam Foundation, Cancer Center Amsterdam welcomed its second robotic system, the state-of-the-art da Vinci XI, in 2021.

Prof. Marc Besselink and the HPB surgery team at Amsterdam UMC have successfully introduced the complex Whipple procedure at Cancer Center Amsterdam and other expert centers in the Netherlands. Now, surgeons from leading hospitals in Europe and beyond are visiting Amsterdam to learn this advanced robotic-assisted pancreatic surgery procedure within the European LEARNBOT program

"From all over Europe and even further away, surgeons visit Amsterdam UMC to learn the latest skills in robot-assisted Whipple procedure." Prof. Marc Besselink

50 teams from the largest hospitals in Europe - including leading centers in Milan, Stockholm, Paris, Berlin, Heidelberg, and Copenhagen - have visited Amsterdam UMC – Cancer Center Amsterdam to learn the procedure.

Prof. Besselink: "It is very inspiring to us all, knowing that patients with pancreatic cancer are receiving the best current clinical practice all over Europe, and even further away, all because of surgical training at Amsterdam UMC – Cancer Center Amsterdam."

Use case Spotlight on Person-Centered Care

By shifting the focus from solely treating the cancer to considering the whole person, healthcare providers can deliver more personalized and effective care that makes a positive impact on quality of life.

Healthcare has recently been undergoing a transformation towards a fully person-centered service model that puts patients at the forefront of their own care. This shift in approach recognizes the importance of involving patients and their families in decision-making, understanding their unique needs and preferences, and tailoring healthcare services to meet those specific requirements. However, there is still a gap between this vision and current practice. To bridge this gap, Cancer Center Amsterdam is researching best practices and innovative approaches in supportive care to improve quality of life for our patients.

At Cancer Center Amsterdam, an integrated team of clinical researchers is working to identify evidence-based improvements in care provisions that will enhance the quality of life for patients with cancer. In recent years, important research lines have been developed in person-centered care like fatigue management in patients with brain tumors (GRIP program), improving shared decision-making, elevating palliative care, and the involvement of family members in care for cancer patients.

1. **Improving Shared Decision Making**

Research has consistently demonstrated that adopting a person-centered approach in healthcare leads to improved patient satisfaction, better health outcomes, and enhanced quality of life.

The positive impact of person-centered care on patient satisfaction has promoted the practice of *shared decision-making*, where healthcare providers and patients collaborate to make informed treatment choices that align with the individual's goals and values.

However, in practice, shared decision making is not so straight forward, according to Inge Henselmans, assistant professor of Medical Psychology at Cancer Center Amsterdam.

“From observational studies at Amsterdam UMC, we discovered that oncologists frequently omit discussion of various options, survival benefits, or the choice to decline treatments with their patients,” says Inge. “A conversation about the value and preferences of the patient was not (or hardly) taking place.”
Together with colleagues from medical psychology and medical oncology including Profs. Hanneke van Laarhoven and Ellen Smets, Inge launched a series of studies beginning in 2015 to investigate ways to improve shared decision making (see text box).

Durable Improvements in Doctor-Patient communication

A key finding arising from these studies was that a training program in shared decision making for oncologists had a significant effect on doctors' communication behavior in the consultation room. “Even months after the training, we observed that doctors acted differently," says Inge. “The level of shared decision making was twice as high as the average reported in literature, and patients also reported a higher level of collaborative decision making.”

This finding highlighted the need for more widespread implementation of shared decision-making skills training. Inge and her colleagues are continuing to examine

the most effective and efficient way of training oncologists, general practitioners, and nurses in shared decision-making skills.

“We are also paying attention to what is best for the patient. On one hand, we want patients to help improve care, share responsibility, and think for themselves. They are the most important member of the team, after all,” says Inge. “But for some patients, shared decision making can actually be an additional burden. We are working on ways to identify and help those patients who need stronger guidance in making decisions from experienced clinicians they can trust.”

Cancer Center Amsterdam projects aimed at improving shared decision making

CHOICE study (KWF Bas Mulder Award, PI Dr. Henselmans; completed 2019) – A randomized controlled trial to evaluate the effectiveness of communication interventions by examining both the separate and combined effect of shared decision-making training for medical oncologists and a patient communication aid in the palliative setting.

SYMPHONY study 2018-2023 (ZonMw, PI Dr. Henselmans; completed) - Interventions for oncologists, general practitioners, nurses and patients aimed at co-determination in the palliative setting. **Winner of the Cancer Center Amsterdam Clinical Impact Award 2021.**

SOURCE study 2022-2026 (KWF, PI Prof.Van Laarhoven; ongoing) – A prediction tool and training program for oncologists to properly inform and collaboratively decide on treatment for patients with esophageal gastrointestinal cancer.

PARADOX study 2022-2026 (KWF, PI Dr. Hillen and Dr. Henselmans; ongoing) – A study of the burden of collaborative decision making for patients with breast/prostate cancer.

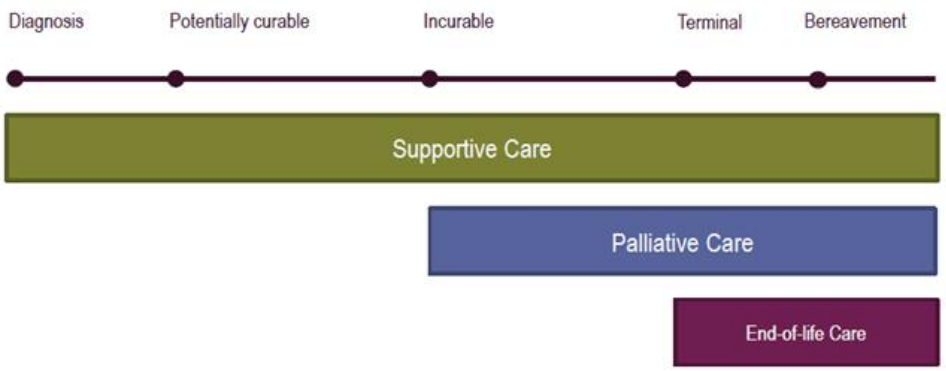
2. A Fresh Look at Palliative Care

Palliative care is an important aspect of person-centered care. It is a specialized approach to care that focuses on improving the quality of life for individuals facing serious illnesses or conditions. Palliative care aims to provide physical, psychological, social, and spiritual support to patients and their families throughout the illness trajectory, including during end-of-life stages.

Attention to palliative care - and the gaps in palliative care provisions - has been increasing rapidly in the Netherlands over the last several years. Cancer Center Amsterdam has taken a leading approach to improving palliative care with the establishment of a theme group ‘Supportive Care’ to bring together researchers who share common interests and who can potentially enhance each other's research. Cancer Center Amsterdam has also appointed Lia van Zuylen, professor at the Kuria Chair Clinical Palliative Care, as leader of the theme group. Supportive Care also works closely with the Expertise Centre Palliative Care Amsterdam UMC to support researchers in evaluating, developing, and implementing interventions and programs for patients with advanced cancer that help optimize the patient’s quality of life.

Additional challenges include a lack of appropriate staffing and dedicated outpatient clinics, sufficient cooperation between caregivers, including GPs, and the need for uniform education to improve the provision of supportive and palliative care. “We must strive to ensure that every patient has access to this important additional layer of support.”

"Traditionally, hospital care is usually focused on diagnosis, treatment, and discharge," says Prof. Van Zuylen. "Several studies have found that supportive care is seriously lacking for oncology patients, especially end-of-life care."



Source: European Society for Medical Oncology

"After all, without quality of life, surviving cancer or living with cancer has no meaning. We need to consider the physical, psychological, social, and spiritual needs of patients to provide the best possible care." Prof. Lia Van Zuylen.

Amsterdam UMC - Cancer Center Amsterdam is also involved in the push towards the development of nationwide quality standards and an education program for all healthcare professionals to improve the quality and effectiveness of supportive care. The role of Amsterdam UMC's Institute of Education and Training is to lead and coordinate the development of training courses in oncological palliative care building on existing initiatives, supported by funding from Dutch Cancer Society (KWF).

The eHealth application 'Oncokompas'

Palliative care is increasingly recognized as an integral part of cancer care. Also, there is growing interest in self-management and behavioral intervention technologies to improve (access to) palliative care. Evidence on the effects of these interventions in palliative care is promising but limited. The application Oncokompas was developed by Cancer Center Amsterdam researchers to monitor physical, psychological, social and existential domains of quality of life, to provide personalized information on quality of life, and to support cancer patients to adopt an active role in managing their disease, adjusted to their personal well-being and preferences.

3. Empowering Families in the Care Process

In person-centered care, the involvement of a patient's family is crucial and highly valued. Cancer Center Amsterdam recognizes the importance of the family unit in a person's well-being and aims to engage and support family members as active participants in the care process.

Originally trained as a nurse, Dr. Anne Eskes is now a principal investigator focused on family engagement. "Families are the very heart of the crucial support network that many patients with cancer need," says Anne. "Traditionally in

healthcare, the focus is solely on the patients and curing the disease. But engaging the families can unlock so much more, from improving shared decision making to active participation in a person's care."

Anne is leading a research program exploring training family members to care for a loved one who undergo cancer surgery. Willing family members are invited to a post-surgical 5-day training program that involves staying in the hospital 24 hours a day. They receive education on medication administration, symptom management, or other aspects of care. "We are equipping them with the necessary skills to assist in the patient's care at home," Anne says.

Training family members to provide care at home has several key advantages

that can improve a patient's quality of life, including improved continuity of care, increased comfort, and a sense of security and independence. It can also help reduce the financial burden associated with professional caregiving services.

Anne points out that family caregivers also face challenges. "It is important to maintain a balance. Serving as a caregiver for a family member can be emotionally challenging and there is a risk of caregiver burnout. So we also look at that."

In the pursuit of person-centered care, recognizing and harnessing the strength of families can truly transform the care experience by fostering a and supportive environment that maximizes the well-being of both patients and their loved ones. Through ongoing research and innovation, Cancer Center Amsterdam continues to refine and enhance family engagement practices, ensuring that families remain at the core of compassionate and effective healthcare.

Use case Spotlight on CAR-T cell Therapy

CAR T-immunotherapy is a type of cancer treatment in which the patient's own immune system is weaponized so it can eliminate cancer cells. T-cells are white blood cells, a type of immune cells that travel in the bloodstream and lymphatic circulation. When T-cells come into contact with a foreign substance or invading entities, they become activated and use their T-cell receptors, a kind of antennae, to detect foreign antigens presented by the patient's own cells and attach to these cells. Once attached, the T-cells can punch holes in an infected cell and inject toxic proteins that cause the cell to die. When normal cells transform into tumor cells, abnormal cellular processes may trigger T-cell activation by recognition of foreign antigens on the tumor cell surface. However, as cancer evolves within a patient, the T-cells may not sufficiently recognize the malignant cells as being 'foreign'. CAR T-cell therapy has been developed to 'arm' the T-cells with chimeric antigen receptors (CARs) which are antennas that can recognize antigens on tumor cells. The CAR T-cells can thus 'track and trace' the tumor cells and destroy them. The CAR T-cell construct also contains a costimulatory molecule which allows for activation of the cells. CAR T-cell treatment starts with extracting T-cells from the patient's blood. In a laboratory, the T-cells are then genetically modified using a harmless virus that introduces a new DNA code with instructions to express the CAR. The CAR locates to the surface of the T-cell (now

a CAR T-cell) and recognizes specifically the cancer cells. When returned to a patient through an infusion into the bloodstream, these CAR T-cells bind to the malignant cells and kill them. One CAR T-cell can kill multiple cancer cells. The CAR T-cells can also expand in the patient, maintaining their CAR-T superpower to recognize and destroy cancer cells. The CAR T-cells stay in the body for a long time after the infusion, helping to keep the patient in remission by fighting cancer if it returns. For this reason, CAR T-cell therapy is usually administered only once. CAR T-cells can therefore be considered a 'living drug'.

PROVIDING CLEAR INFORMATION AND IMPROVING THE QUALITY OF LIFE

Marie José Kersten, Professor of Hematology, has lobbied at the national level for the introduction and implementation of CAR T-cell therapy in the Netherlands, including getting this treatment reimbursed. She also coordinates Amsterdam UMC's involvement in several large national and international research consortiums. In 2020, Prof. Kersten obtained multiple research grants to implement CAR T-cell therapy faster for more patients and investigate the impact of this immunotherapy on patients' well-being and quality of life. Prof. Kersten explains: "CAR T-cell therapy does not work for everyone: only forty percent of treated patients have long-lasting benefits. We want to develop materials that support the patient during the entire process. It is precisely the voice of the patient and informal caregiver we listen to: what is needed to better guide them during that 'voyage'?" The goal is to determine the best way to educate patients, their support team, and treating physicians so that everyone knows what they can expect before, during, and after the treatment.

CAN IN-HOUSE CAR T-CELL THERAPY SAVE TIME AND MONEY?

A consortium of academic hospitals in the Netherlands, headed by Tom van Meerten from UMC Groningen, and including Amsterdam UMC, Radboud UMC, and Erasmus MC, received a € 30 million subsidy from Zorginstituut Netherlands and ZonMw in 2020. The academic centers plan to compare in-house CAR T-cell production with commercial sources to see if savings in time and costs can be achieved. Marie José Kersten is also involved in this project. "A quicker throughput time is very important to these patients. It's precisely this group who needs the treatment fast because they don't usually have other options and have rapidly progressive disease, which is sometimes prohibitive for CAR T-cell therapy due to the waiting time during manufacturing," says Prof. Kersten. Faster and cheaper CAR T-cell production would also significantly improve accessibility for more patients. Currently, treatment per patient costs around €350,000 for the cells and the consortium aims to reduce that to € 80-100,000. CAR T-cell therapy is so expensive because the entire treatment must be developed from start to finish for each patient individually. It also takes about four to six weeks before the lab-engineered immune cells can be given to the patient using an international commercial partner. Some patients simply do not have that time. The consortium aims to reduce production time to two weeks, as well as possibly improving the quality of the CAR T-cells by avoiding the freeze-thaw processes necessary for shipping.

Appendix 23: Run for the region

September 15, 2022

New network for cancer research with regional hospitals

A Unique Initiative' Collaborative Regional Research Network

Cancer Center Amsterdam and Antoni van Leeuwenhoek Ziekenhuis are working together with hospitals in the North Holland & Flevoland region to establish a centralized oncology research network. This collaborative approach allows greater sharing of resources, knowledge, and expertise, which can lead to more innovative ideas and breakthroughs in cancer research.

"What this project aims to do is create a centralized network with hospitals and patients coming together in oncology research," says Prof. Sonja Zweegman, project leader and vice-chair of Cancer Center Amsterdam. "This is a unique initiative! We are harnessing the power of collaboration to do research faster and more efficiently with each other."

Supported by a grant from the Dutch Cancer Society (KWF) of 2.4 million euros, the 'Ren voor de Regio' (Run for the Region) project first aims to establish the infrastructure and harmonize protocols necessary to support a collaborative research network.

"We will be collaborating with Antoni van Leeuwenhoek Ziekenhuis on all aspects involved with cancer research. For now, we are working to align our procedures to swiftly and efficiently initiate and conduct clinical research in the region," says Wendy Onstenk, program manager. "We need to establish a thorough organization of the infrastructure. That's why we are starting with only a few hospitals in this pilot phase. In the second part of the project, we will expand and invite all other hospitals to join us and further develop towards a true region-wide network."

> *"As the majority of early clinical trials are currently being conducted in university medical centers, an increasing number of cancer patients who are treated in the region miss out on novel, potentially valuable treatment options within the framework of a clinical trial." - Prof. Sonja Zweegman, project leader and vice-chair of Cancer Center Amsterdam*

'A great new opportunity'

For the first phase of the project, which started in December 2022, the collaboration will include seven hospitals: OLVG, Flevoziekenhuis, Dijklander ziekenhuis, Spaarne Gasthuis, Noordwest Ziekenhuisgroep, AvL, and Amsterdam UMC.

The Dutch Oncology Research Platform (DORP) has also partnered up to establish the formal and logistical backbone, and Integraal Kankercentrum Nederland (IKNL) is involved for local data management solutions.

A regional research team

The KWF-funded project supports the appointment of a regional research team. A central project coordinator will be stationed at Amsterdam UMC and liaison with local study coordinators who will work from different hospitals in the region. A team of medical students will provide hands-on support when needed, under the supervision of local coordinators.

The regional research team will be responsible for logistics, communications, and coordination, in addition to supporting the initiation of trials and raising awareness of clinical studies across the region. “This unique set up assures better access to innovative therapies for all cancer patients in need of new treatments across the region - not only for those attending Cancer Center Amsterdam or Antoni van Leeuwenhoek Ziekenhuis,” says Wendy Onstenk.

More than clinical trial research

The ‘Ren voor de Regio’ project is more than just increasing patient participation in clinical trials. A centralized biobank infrastructure will also facilitate the collection and availability of biobank samples from patients with stage I-IV disease for research. In addition, a regional data governance structure will be installed in collaboration with Health-RI to make healthcare data available for retrospective data research.

“Also, if patients are referred to us for specialized or complex care and then return to the local care provider, we want to make sure they don’t disappear from a clinical study, but can be followed up in those regional hospitals,” adds Prof. Jan Paul Medema, Director of Research at Cancer Center Amsterdam and co-principal investigator of the project.

“Data and sample collections will help expedite the development and validation of improved treatments and (diagnostic) tests, and in a positive feedback loop, will offer improved and innovative treatments to cancer patients across the region. Everybody is really seeing this as a great new opportunity.” Prof. Jan Paul Medema, Director of Research at Cancer Center Amsterdam and co-principal investigator of the project.

Expanding joint biobanks is important because this boosts the chances of finding new biological insights. “There is still so much we do not know. Research based on biobanks holds great promise to reveal new ways to detect, treat, and monitor cancer for current and future patients,” explains Wendy. “The more patients participate in research, the better we can unravel the biological complexities that underlie cancer. More participants at all disease stages means better statistical power to uncover new patterns and correlations to improve or identify new treatments.”

Regional Network for Oncology Research

Supported by funds raised through the KWF Run Against Cancer campaign with the TCS Amsterdam Marathon**,** the 4-year Regional Network for Oncology Research (Ren voor de Regio) project aims to:

- Coordinate and facilitate clinical trials across the region to increase patient participation and expand access to innovative treatments
- Increase sample provision to joint biobank projects including the Cancer Center Amsterdam-initiated Liquid Biopsy Center
- Optimize data collection from cancer patients, from diagnosis to long-term follow up, by harmonizing collection and registration of health data
- Create a regional data- and biobank covering all cancer patients to
  - provide insight into real world data and allow comparison of standard-of-care to more experimental treatments
  - enable data sharing across the region
  - facilitate our understanding of disease biology and therapy efficacy
  - decrease selection bias by included patient data from non-academic hospitals

Collaborative Regional Care and Research Network in Oncology

By working with other hospitals and research institutes in the region, we can accelerate the pace of cancer research, reduce the cost of cancer care, and improve the patient's experience.

Cancer Center Amsterdam's mission is to create ground-breaking new possibilities for patients with cancer. One of the ways that the center achieves that mission is through its active and committed participation in regional networks for cancer care and research.

Trailblazing Regional Care Pathways

The Integral Care Agreement (IZA) is a four-year agreement between the Dutch government and the healthcare sector, signed in September 2022. Two of the IZA's aims are to 1) concentrate complex care at fewer, specialized hospitals and 2) improve the coordination of care between different healthcare providers. This will make it easier for patients to get the care they need, when they need it, and will also help to improve the quality of care.

"For complex surgery, patients go to a specific location that specializes in that operation, while standard care or follow-up care can be provided by their own GP or local hospital around the corner." Prof. Geert Kazemier, Chair Executive Board Cancer Center Amsterdam.

Cancer Center Amsterdam, one of the two designated regional hospitals specialized in complex care, has taken the leadership in establishing guidelines for the coordination of care between different regional healthcare providers - 'care pathways'. Care pathways have been established and are currently operational for several tumor types (with more to come):

- Improving care for patients with liver tumors via a regional care pathway

Long-Term Regional Collaborations

Cancer Center Amsterdam has been cooperating in regional and national networks for cancer care for over 20 years.

One example of this are **tumor boards:** multidisciplinary teams of experts who meet regularly to discuss the treatment of patients with specific types of cancer. These teams bring together oncologists, surgeons, radiologists, pathologists, and other specialists from various hospitals and universities to ensure that patients receive the most comprehensive and up-to-date care possible.

Cancer Center Amsterdam has been instrumental in establishing and/or participating in:

- The Prostate Cancer Network
- Gastrointestinal Oncology Center Amsterdam (GIOCA)
- Hemato-Oncologie voor Volwassenen Nederland
- Center for Gynecologic Oncology Amsterdam
- Brain Tumor Center Amsterdam
- The Dutch Pancreatic Cancer Group (DPCG)
- Dutch Upper GI Cancer Group (DUCG)
- The National Working Group on Neuro-oncology (LWNO)
- European Head and Neck Surgery Tumor Board
- Oncology Networks Netherlands

"By working together, this can make a real difference in the lives of patients with cancer." Geert Kazemier, Chair Executive Board, Cancer Center Amsterdam.

- Seven distinct regional gastrointestinal oncological care pathways Centralization empowers super-specialists in cancer healthcare
- Lung Cancer / 'Less practice variation, more optimal care'
- And an App that provides detailed information on established regional care pathways including all the contact details of healthcare professionals involved

Regional Research & Care: To the Future, and Beyond

In hand with the redistribution of (specialized) care and greater regional coordination as part of the IZA, an overarching regional oncology network will be launched in 2023.

This network, OncoNoVo+, is a partnership involving Antoni van Leeuwenhoek (AvL), 13 regional hospitals, general practitioners, primary care providers, ZBCs, and patient associations. The aim is to join all forces to jointly shape the future of oncological research with patients in the North Holland/Flevoland region.

The aim is to join all forces to jointly shape the future of oncological research and care in the North Holland/Flevoland region."

Prof. Marc Besselink, Member OncoNovo steering committee, Cancer Center Amsterdam.

This collaborative approach underlying OncoNoVo+ allows greater sharing of resources, knowledge, and expertise, which can lead to more innovative ideas and breakthroughs in cancer research.

Already, the regional research infrastructure is being established with the support of a Cancer Center Amsterdam-led KWF-subsidized project "Ren voor de Regio" (Run-for-the-Region). This will support expansion of clinical studies throughout hospitals in the network. By increasing participation in clinical trials, more patients will have the opportunity to receive the latest treatments in a research setting.

At the end of the four-year project, the research infrastructure is expected to be embedded within OncoNoVo+ to seamlessly connect care and research in the region.

Appendix 24: Patient Research Groups

Patient Research Groups	Short description	Main focus/Aims for coming years
Breast Cancer	The PRG Breast Cancer is a multidisciplinary team consisting of dedicated breast cancer professionals including surgical, medical and radiation oncologists, nurse practitioners, breast care nurses, radiologists, nuclear medicine doctors, plastic surgeons, clinical genetics, gynaecologists for fertility preservation and AYA-professionals. All professionals work on clinical departments with high standards for breast cancer care and research, and have a close collaboration in the region (i.e. Flevo-, Amstelland, Dijklander ziekenhuis and Zaans Medisch Centrum). We have regular meetings to discuss the quality of breast cancer care, such as clinical problems, clinical guidelines, numbers, and new and (preliminary) results of clinical trials.	There is a close collaboration within the PRG breast cancer professionals and translational research together with the group leaders from Cancer Biology and Immunology, LEXOR and CEMM labs, and Hyperthermia group. In the coming years, we will continue to focus on the optimization and personalization of breast cancer imaging and treatment in multicenter studies. These are: • MRI-guided single-dose preoperative radiotherapy including response monitoring (MRI, biomarkers) in low-risk patients (KWF ABLATIVE project). • Preoperative radiotherapy before reconstructive surgery (BRENAR project). • Optimization of postoperative re-irradiation+/-hyperthermia in locoregional recurrent breast cancer (KWF RT-HYPE project). • PET-imaging as part of diagnostics and treatment evaluation, with focus on FES-PET and molecular imaging (CCA Foresight trial, KWF SONImage tiral, ALpeDHuzes IMPACT project). • Participation in national studies that focus on personalization of treatment (e.g. KWF DESCARTES, KWF LORD trials) and shared decision making.
Dermato-Oncology	As multi-disciplinary patient-research group within a melanoma center, we strive to optimize local and systemic treatment for patients with stage I-IV melanoma through research aimed at improving efficacy and mitigating toxicity, such that patients have the best chances of favorable outcome and good quality of life. The PRG actively collects peripheral blood and patient tissues to enable translational and immunomonitoring studies focusing on response, toxicity and the antitumor activity of vitiligo. Integrating basic, translational and clinical research locally, regionally and (inter)nationally, we stimulate interaction and knowledge exchange between researchers, and support joint research projects and grant applications.	• Locoregional TLR9 agonist or low-dosed checkpoint inhibitor administration to enhance immune activation locally, in the draining lymph node, and systemically in stage I-IV melanoma • Monobenzone/imiquimod-based induction of vitiligo to improve melanoma specific immunity and potentiate efficacy of checkpoint inhibition in advanced melanoma • Identification of predictive biomarkers for response and toxicity to checkpoint inhibition using clinical characteristics, blood tests and genome wide association studies (GWAS) in patients with advanced melanoma • Analysis of the relation between genomic alterations and the tumour immune contexture in immunotherapy resistant patients with advanced melanoma • Analysis of real-world outcome data of patients with stage III-IV melanoma in the Netherlands (Dutch Melanoma Treatment Registry) • Checkpoint inhibitor-induced (skin, rheumatic, gastro-enterological, cardiac and endocrine) toxicities in patients with stage III-IV melanoma; improving risk stratification and treatment
Gynaecological Oncology	Because gynaecological cancers are rare tumours, care for women with gynaecological cancer is centralized. We are one of the 9 specialized gynaecological oncological centers in the Netherlands, receiving referrals from a large region (from Deventer to Den Helder). We collaborate closely with other medical specialists (e.g. medical oncologists, radiation oncologists, pathologists etc) in both patient care and research. Our research endeavors vary from basic science to clinical trials. In 2022 we were acknowledged as an Expertise center for rare disorders (ECZA).	• Treatment of cervical cancer, with specific focus on fertility-sparing surgery (one of the two in NL). In general, we have specific expertise in treating women with cancer and wish to preserve fertility or treating pregnant women with cancer. • Late effects after treatment: we established a multidisciplinary team to provide care who suffer from late effects after multimodal treatment for gynaecological cancer (ELEGANT poli) • Focus on improvement of lifestyle (e.g. stop smoking) in women with cancer • Strong collaboration with basic researchers. Examples: local immunotherapy in cervical cancer (prof dr T. de Gruijl) and DNA methylation analysis in different types of gynaecological cancer (prof dr R. Steenbergen, dr M. Bleeker). • Holistic approach of care for women with gynaecological cancer: both in clinical care and in research, including themes such as personalizing care, using PROMs, shared decision-making and AI. We specifically also focus in these projects on women with low (health) literacy and varying cultural backgrounds, corresponding to the diverse makeup of the Amsterdam UMC patient population.

Head and Neck Oncology	The patient-research-group head-and-neck-oncology (PRG-HNO) comprises all patients with a tumor in the upper-aerodigestive tract and other structures in the head and neck, including cutaneous tumors. This anatomical region includes the facial structures, the blood supply to the brain, the cranial nerves, as well as the organs for nourishment, respiration, and communication. The complex anatomy and important physiology impact the treatment strategies that can be applied. The malignancies in the head and neck encompass a large variety of tumors including cutaneous and mucosal melanomas, but also salivary gland tumors, sarcomas and neurogenic tumors. The very large majority of malignancies (>90%), however, are squamous cell carcinomas (HNSCCs) originating in the mucosal lining. These are caused by exposure to carcinogens, infection with the human papillomavirus (HPV), and genetic predisposition, most particularly Fanconi anemia.	The major research focus is on HNSCC and the different etiologies that translate into different molecular tumor classes. In addition, high precision treatment, value-based healthcare and improving survival and quality of life remain important focus areas, particularly in the context of immunotherapy that opened new horizons in head and neck oncology. In addition, treatment resistance is a major research focus both in the context of intratumor heterogeneity and tumor-microenvironment interactions. Also early diagnosis and disease monitoring by e.g. ctDNA in liquid biopsies are an important topic. The unique origin of HNSCC in large fields of precancerous mucosal changes, which are sometimes visible as white patches (leukoplakia), forms a research topic for early diagnosis, risk stratification and development of novel treatments, the latter both by collaboration with pharmaceutical industry but also by drug repurposing strategies.
Lung Cancer	Our multidisciplinary research group involves professionals from various backgrounds, such as thoracic oncologists, thoracic surgeons, radiation oncologists, pathologists, nuclear medicine physicians and radiologists, as well as preclinical researchers from the Cancer Immunology theme. The clinical departments, including radiation oncology, pulmonary diseases, thoracic surgery, and pathology, are all dedicated to providing the best care for lung cancer patients, and are also deeply involved in the ongoing research to optimize the treatment of patients with lung cancer. Together with the group leaders from different Cancer Immunology labs, our PRG conducts translational research, and multiple clinical (multimodal) studies, with particular focus on the role of immunotherapy. The research team is jointly facilitated and completed by the collaboration with the Radiology and Nuclear Medicine Department. For this purpose, the most innovative modern imaging tracers are developed and implemented in the clinic, while state-of-the art machines are used to perform high quality scans. We regularly discuss ongoing projects in alternating core and broader team meetings, attended by both preclinical and clinical researchers, striving to align our activities while maintaining independence. Our clinical studies supply biomaterials to preclinical researchers from four PI groups with complementary expertise, who in turn provide fundamental input to guide future study directions. Additionally, our group is heavily involved in PET-imaging research, which is often integrated into joint clinical studies, focusing on staging, restaging and response evaluation after different therapeutic approaches. This also includes immune monitoring. Furthermore, our group explores various monodisciplinary topics, such as endobronchial interventions using navigational bronchoscopy, confocal laser endoscopy, and endobronchial anticancer therapies; personalized therapy studies; quality of life and palliative care studies; pharma-sponsored clinical trials; biobanking of blood, tissues, and single cells; patterns of care research, and more.	We aim to: • Explore multimodal immunotherapy studies, examining pathological and clinical responses to chemo-immunotherapy, radio-immunotherapy, and dual immunotherapies in early-stage and metastatic non-small cell lung cancer (NSCLC) • Incorporate regular immune profiling of blood (and lymph node and tumor tissues) in the design of clinical trials for consistent immune monitoring • Assess the role of lymph nodes in the immune response to tumors, as well as their role in enhancing the effectiveness of anti-cancer therapies • Utilize 40-stain advanced multiplex imaging of the tumor microenvironment to explore cellular interactions and spatial relationships • Utilize a bioinformatic approach to the tumor microenvironment using deconvolution algorithms and tumor cellular states resulting in classification of tumors into prognostic and predictive eco-states with distinct tumor microenvironments and therapeutic vulnerability • Utilize immuno-PET imaging to visualize and quantify key players in the immune microenvironment, aiding in the development of immunotherapy-based treatment strategies • Continue dedication to monodisciplinary focus areas, ensuring in-depth research and development in each specific field

Lymphoid Malignancies	The lymphoid PRG has three central themes: studying mechanisms of resistance, developing (combinations of) targeted therapies based on specific vulnerabilities of the tumor within its microenvironment, and immunotherapeutic strategies directed at the tumor cells. These themes are applied on multiple myeloma, lymphoma and CLL. Execution and development occurs within frameworks for novel therapeutic, diagnostic/imaging and experimental tools. Some highlights: CLL: development of 3D spheroid model to study TME interactions and perform drug screens study T cell dysfunction from metabolic perspective, develop new immunotherapies Lymphoma: -Delineate MYC induced immune escape mechanism, delineate CDC resistance -Improve immunotherapies by new antibodies (bispecifics, hexabody and CAR-T)	Explore multimodal immunotherapy studies, examining pathological and clinical responses to chemo-immunotherapy, radio-immunotherapy, and dual immunotherapies in early-stage and metastatic non-small cell lung cancer (NSCLC) • Incorporate regular immune profiling of blood (and lymph node and tumor tissues) in the design of clinical trials for consistent immune monitoring • Assess the role of lymph nodes in the immune response to tumors, as well as their role in enhancing the effectiveness of anti-cancer therapies • Utilize 40-stain advanced multiplex imaging of the tumor microenvironment to explore cellular interactions and spatial relationships • Utilize a bioinformatic approach to the tumor microenvironment using deconvolution algorithms and tumor cellular states resulting in classification of tumors into prognostic and predictive eco-states with distinct tumor microenvironments and therapeutic vulnerability • Utilize immuno-PET imaging to visualize and quantify key players in the immune microenvironment, aiding in the development of immunotherapy-based treatment strategies • Continue dedication to monodisciplinary focus areas, ensuring in-depth research and development in each specific field
Myeloid Malignancies	Our myeloid PRG has a bi-weekly meeting with hematologists, research nurses, members of the trial bureau and a laboratory specialist. We have predefined agenda points including ongoing studies: Progress and specific relevant details; New and planned studies: Progress of procedures (staff approval, budget, clinical and laboratory requirements, contracts etc.); Issues or specific requests from, or for, the laboratory (Biobanking or specific assays); Collaboration within the team and communication; Patients: potentially eligible for studies and/or current status; Presence or specific absences (conferences etc.). The meeting is in person and virtual to ensure most participant to be able to join.	There are many novel treatment modalities for the acute myeloid leukemia and high myeloid dysplastic syndrome (MDS) risk patients and we will focus on selecting those that are most promising for our patients and best aligned with research in our department. This includes novel drugs (currently implementation of venetoclax in myeloid malignancies) and drug combinations but also cell therapy such as NK-cell vaccinations. In addition, we anticipate to find good markers for CAR-T cells and/or other targeted (antibody) therapy. To assess treatment response we focus on measurable residual disease assessment by flow cytometry, ideally monitoring the aberrant cells and the treatment target. For MDS emphasis is currently also on risk classification to tailor treatment. For chronic myeloid leukemia we focus on assessing when a patient can stop with the treatment and try to find biomarkers to identify patients that are eligible to stop.
Neuro-endocrine Neoplasms	The neuroendocrine neoplasms (NEN) PRG is a multidisciplinary team dedicated to providing excellent care for patients with these rare tumors. Current name should be NEN since this includes the neuroendocrine tumors (NET) and neuroendocrine carcinoma's (NEC). We are an ENETS (European Neuroendocrine Tumor Society) accredited center, one of 5 centers in the Netherlands and were accredited again in 2023. We are also an NFU/ERN-EURACAN rare disease center. Our team of specialists includes surgeons, medical oncologists, endocrinologists, gastroenterologists, radiotherapists, radiologists, interventional radiologists, nuclear medicine physicians, pathologists and a new nurse specialist.	The main focuses of the PRG concerns further strengthening of basic and clinical research. Focuss concerns mainly oncological studies for Net and NEC patients and clinical studies in PNET and small bowel NET patients. Fluorescence, operation techniques, PRRT treatment, molecular biology for risk stratification are current projects. Collaborations are important and include the Dutch Pancreatic Cancer Group (DPCG) Dutch-Belgian Network, FORCE working group and new collaborations with UMC Utrecht on molecular biology. Also international collaborations are important with for example the ENETS-MEN1 workgroup and the small bowel NET registry.

Neuro-Oncology	The following departments are involved in the neuro-oncology PRG: Neurology, Neurosurgery, Radiotherapy, Medical Oncology, Pathology, Medical Psychology, Anatomy and Neurosciences (ANW). All departments, with the exception of ANW are involved in patient care, which displays the collaborative nature of clinical neuro-oncology. This is also reflected in the numerus collaborative research efforts of the neuro-oncology PRG. Our Research consists of: Investigator initiated clinical trials, Clinical outcome effect studies , Participation in industry driven clinical trials, Pre-clinical / translational lab research, Imaging, neurophysiological and network neuroscience research, including biomarker discovery Cognition /quality of life studies in glioma patients.	<u>Patient Care</u> The brain tumor center Amsterdam is part of the European reference network (ERN) for rare diseases and as such recognized as European center of expertise for brain tumors. The focus in patient care is on adult primary and metastatic brain tumors. <u>Research</u> The mentioned research has been focused on high and low grade glioma, for the future this focus will remain. More specifically the following studies and research lines are planned for the coming years: Liquid biopsies for monitoring glioma pseudo-progression; Target identification and drug (combination) development for high grade glioma; Computational biology of glioma; Cancer neuroscience on how the tumor and brain interact; Multiscale network neuroscience aiming to relate cellular effects of tumors to large-scale brain networks and patient functioning and cognition; Multimodal imaging to improve local treatment of glioma; Intra operative ultrafast molecular diagnostics for glioma
Pancreas Cancer	PRG pancreatic malignancy deals with multidisciplinary care for pancreatic carcinoma. We have weekly 2 MDOs where all patients with (suspected) pancreatic carcinoma are discussed and a plan is drawn up in consultation with surgery, oncology, MDL, radiotherapy, radiology. In addition, very active research is conducted.	Main focus in research is on neoadjuvant treatments (chemo and radiotherapy), surgical approaches (open vs minimally invasive surgery), radiotehrapy, palliative treatments in terms of pain relief, bile duct drainage (ERCP vs EUS guided).
Primary liver and bile duct Cancer	This PRG consists of gastro-enterologists, surgeons, pathologists, interventional radiologists, radiologists, allied healthcare givers, and oncologists who diagnose and/or treat tumors of the liver and bile ducts. We have two separate MDTs both on the same day (Monday) and collectivemultidisciplinary outpatient clinic. The primary liver tumor part includes mainly patients with hepatocellular carcinoma (HCC), including specific subtypes , ie fibro lamellar carcinoma, and EHE'sbut also benign liver tumors, which may require treatment such as adenomas, complicated liver cysts or symptomatic hemangiomas' or soft tissue tumors of unknown origin. the bile MDT coversall biliary tract cancer (BTC) subtypes with the exception of resectable distal Cholangiocarcinoma which is discussed in the pancreas MDT. Our center is a certifiedexpert center on a national (NFU) and international level (EURACAN). We comply with SONCOS and the most recent (inter) national guidelines.	To offer our patients the best "word class" care available. To improve outcomes for current and future patients withhepatic and biliary tumors. (Trials and research) To train students, allied healthcare workers and medical professionals To review and improve our performance in a continuous improvement cycle.
Retinoblastoma	Since 1991, Amsterdam UMC has been serving as the national referral center for patients with retinoblastoma in the Netherlands. The team of experts from different fields is responsible for diagnosing, treating and monitoring children with this hereditary form of eye cancer. The primary objective of their treatment is to preserve the life of the patient and, if possible, their vision and eye, with a focus on maintaining their quality of life while minimizing any late effects of treatment. This multidisciplinary team has established strong clinical and scientific collaborations, and has built a strong (inter)national track record on Rb research.	The main focus of our PRG is to continue as a national referral center and combine the clinical work with translational research. The main focus of our research is on cognitive functioning and quality of life in retinoblastoma survivors, development of non-invasive blood test for early detection of second primary tumors. Furthermore, we will continue our pioneering research on imaging in retinoblastoma with special focus on phenotyping various genetic variations in retinoblastoma and development and global implementation of guidelines on retinoblastoma imaging.

Sarcoma	The PRG “Sarcoma’s” has a multidisciplinary core of medical specialists on primary mesenchymal tumors (radiology, pathology, (orthopedic) surgery, oncology, radiotherapy, rehabilitation) . We have a supra-regional top-referent clinical and consultative function. The biweekly MDT-meeting, with participants from both in- and outside Amsterdam UMC, advises on a wide range of primary and metastatic tumors. Top-referent treatment is given by the multidisciplinary team in cooperation with many others. Apart from clinic, the PRG is active in research and education. We are acknowledged as Center of Excellence (ECZA) on Bone- and Soft Tissue Sarcoma’s by the NFU/VWS in the European Reference Network (ERN).	Main focus coming years is to continue and strengthen our work and research on Bone- and Soft tissue Sarcoma’s as Centre of Excellence. We want to expand activities in Adolescents and Young Adults (AYA’s) with sarcoma’s. Furthermore to elaborate research on diagnostics, treatment and late results (aftercare, functional results, quality of life, shared decision making, results of sarcoma treatment in AYA’s, hypnotic therapy, giant cell tumors, interventional radiology, quantitative diagnostics) and in education in the complete range from medical student to specialist and in adjacent professions on sarcoma’s.
Thyroid Carcinoma	The thyroid carcinoma PRG is a multidisciplinary team dedicated to providing excellent care for thyroid cancer patients in the greater Amsterdam area. Our team of specialists includes pediatric and adult endocrine surgeons, medical oncologists, endocrinologists, radiotherapists, radiologists, nuclear medicine physicians, pathologists, clinical chemists and a nurse specialist. The PRG is a level 1 center for thyroid cancer care, as well as an NFU/ERN-ENDO and ERN-EURACAN certified rare disease center.	The main focuses of the PRG will include optimizing regional care for thyroid cancer patients within the framework of ONCONOVO+, as well as expanding research efforts in particular with regard to improving surgery and endocrine aspects of thyroid cancer treatment.
Upper GI	PRG upper GI oncology deals with multidisciplinary care for gastric and esophageal malignancies. There are 2 weekly MDTs where all patients with (suspected) gastric and esophageal cancer are discussed and a plan is drawn up in consultation with surgery, medical oncology, gastroenterology, radiotherapy, radiology. In addition, very active clinical and basic research is conducted. The Amsterdam UMC has the largest patient volume of patients with upper GI cancer in the Netherlands.	Main focus in research is on neoadjuvant treatment strategies (chemotherapy, radiotherapy and immunotherapy) and surgical approaches (robotic and minimally invasive surgery) and extent of surgery Research is also important in patients with primary non surgical curative treatment and palliative treatments in terms of pain relief and relief of complaints.
Urology	The department of urology of the AmsterdamUMC has four domains of research (PRG’s) within the oncological field: Prostate cancer, Bladder cancer, Kidney cancer, Urothelial carcinoma of the upper tract The PRG’s are active in basic research, new imaging modalities, evaluation of existing scanning modalities, scientific evaluation of quality control in surgical procedures.	We focus on imaging technology, evaluation of minimal invasive treatment modalities. We expand collaboration with other (academic) hospitals and universities. We play a leading role in regional and national collaborative cancer networks.