

# **2021 ANNUAL REPORT**

Oncologie Onderzoekschool Amsterdam
- OOA -











#### **OOA INSTITUTES**









### **About the OOA**

The training and supervision of Amsterdam's PhD candidates working on a project in Oncology is embedded in the Oncology Graduate School Amsterdam (Onderzoekschool Oncologie Amsterdam – OOA). The mission of the OOA is to provide a broad range of high-quality educational courses in oncology, and to ensure proper supervision of PhD candidates working in oncology research in the Amsterdam area. The key strength of the OOA is the fruitful collaboration between two state-of-the-art institutes, Amsterdam UMC and NKI-AVL, which provides PhD candidates the opportunity to learn and collaborate with internationally recognized scientists with in-depth expertise on a wide range of oncological topics. With their help, we maintain a longstanding tradition of almost 30 years offering educational programs with high-quality courses covering a wide range of topics.

The OOA is a large and successful school, home to over 1000 PhD candidates who, next to their research, receive theoretical and practical education on a variety of subjects related to cancer research and treatment. Our professional knowledge courses focus on cutting-edge scientific topics and the core research activities at the associated institutes, covering specific tumor types and topics within oncology, as well as new groundbreaking technologies that will provide the students with the right skills and expertise to apply these methods in their own research. We are also exploring to what extent we can offer psychological support to PhD candidates who experience work-related stress.

The OOA is one of the 23 graduate schools in the Netherlands in the field of 'Life Sciences and Medicine'. It is the only Royal Netherlands Academy of Arts and Sciences (KNAW) accredited school that is specifically focusing on training in fundamental, translational and clinical cancer research.

Due to our focus on oncology and affiliation with cancer treatment centers, we highly value the translation of basic research findings into clinical applications, and vice versa. We therefore stimulate cooperation and integration of fundamental and clinical researchers.

### PhD candidates in 2021

Click here for more details

### 26% international

35% male, 65% female

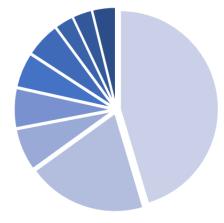
25% of projects funded by the participating institutes

16% by public funds

41% by research contracts

18% financed by other funds

### Pre-education of PhD candidates



- Medicine
- Biomedical/biomolecular sciences
- Biotechnology/technical medicine/engineering
- Pharmacy/drug discovery/(bio)chemistry
- Cancer/Oncology
- Bioinformatics/mathematics/epidemiology/AI
- Health/forensic/movement sciences
- Neurosciences/psychology/sociology
- Other



### Research themes

THEME 1. BASIC ONCOLOGY

The transformation of a normal cell into a malignant cancer cell requires multiple (epi)genetic alterations affecting genes that constitute pathways governing the proliferation and behaviour of cells. Studying the genes and proteins involved in these pathways results in better understanding of tumor development, progression and therapy resistance and may yield markers that can be used to detect cancer at an early stage and to predict its course and response to therapeutic interventions. Disease profiling is being improved using innovative research tools that include high-throughput methods for (epi)genetic, transcriptomic and proteomic analyses. At the cellular level, processes like cell-cell communication, differentiation, adhesion, migration, survival, proliferation and apoptosis are studied using e.g. advanced microscopy, which are complemented by molecular studies using e.g. st@@unanagementy.eam Advanced autochthonous mouse models and sophisticated xenotransplant models have been developed for the genetic dissection of cancer and testing of novel therapeutic strategies, including immunological interventions. Furthermore, the mechanisms of therapy resistance and metastasis are being investigated.

Viral oncogenesis projects focus on the role of human papilloma viruses and Epstein-Barr virus. Viral and host markers are being tested for their capability to assess the risk associated with the development of cancer.

### THEME 2. CLINICAL RESEARCH

Improvements of clinical care are based on improved detection and development of innovative therapies and personalized treatment strategies. The emerging and rapidly growing fields of molecular imaging and genomics are providing new opportunities to study the biology of a malignancy in individual patients and thus allowing for the development of highly valuable indicators for diagnosis and prediction of disease outcome. Modern state-of-the-art techniques like MRI, SPECT, PET and PET/CT enable tumor imaging with high precision and unique molecular and biological information at the tissue level. Mouse models are being used to follow drug sensitivity in several types of cancer and for developing clinical strategies for imaging. Another important focus of research is optimizing the benefits of targeted cancer therapy. Research includes (pre)clinical evaluations of neoadjuvant treatment and the application of new molecular therapies and anti-angiogenic agents against novel targets in the tumor and its environment. The pharmacological optimization of cytotoxic drugs is an important line of research, as is the passage of drugs through the blood-brain barrier. Development of immunotherapies based on immune checkpoint blockades, adoptive transfer and vaccination strategies, as well as identification of predictor response to these therapies are at the forefront of research. Another important research focus is quality of life of long-term survivors of childhood and adult cancer.

The institutes provide state-of-the-art research facilities. New initiatives are being launched and innovative technologies are developed and implemented. This often occurs in the context of research programmes in which PhD students are actively involved. Please click here for an overview of all facilities.

OOA research has an excellent (inter)national status, as demonstrated by the large number of research projects granted in open (inter)national calls, including several of the prestigious new grants. The faculty is strongly represented in the Dutch science foundation (NWO) 'vernieuwingsimpuls', the Veni, Vidi and Vici grants for junior researchers and participated widely in numerous EU integrated projects and networks of excellence. Funding is also strongly supported by the Dutch cancer society (KWF).

### PhD training and supervision

Since EU countries, including the Netherlands, agreed to the Bologna declaration (a three-cycle higher education system consisting of bachelor's, master's and doctoral studies), the educational part of the doctoral program got a more prominent role. At OOA, policies regarding the training and education of PhD candidates have changed considerably over the last few years. In the past, different rules and regulations were in place among the involved research institutes. For example, graduation requirements varied from 30 obligatory education credits (ECTS) to no obligations at all. This resulted in differences in the quality of education OOA PhD candidates received at different locations. To improve this undesirable situation, we have put much effort into aligning the training and education of our PhD candidates over the last two years. In consultation with Amsterdam UMC deans and the NKI-AvL scientific director, we implemented a uniform OOA PhD candidate Training Plan at all three research locations, based on the best practices of the involved institutes.

The main goal is that all Amsterdam-based PhD candidates in oncology acquire and develop the right skills and knowledge that will ensure a successful career, either within or outside academia. Our Training Plan is mandatory for all OOA PhD candidates starting their doctoral research as of January 1, 2021, and includes a number of obligatory educational and training elements essential for every PhD candidate, complemented by a number of optional courses that can be tailored to individual needs, interests and background. The basic criteria of all Training Plans are the same and include:

- A total number of 30 ECTS (1 ECTS equals 28 hours);
- A mandatory 'Ethics and Integrity in Science' course (2 ECTS);
- At least 8 ECTS earned in professional knowledge and general skills courses (including the Ethics course);
- At least one visit to a scientific conference (max 2 ECTS per visit);
- The remaining credits are earned by participating in courses, activities, retreats, conferences, group meetings, student supervision, etc.

Most courses in the PhD candidate educational program are provided by OOA. We have a longstanding tradition of almost 30 years offering educational programs with high-quality courses covering a wide range of topics. The last four years, we

have doubled our activities and will further expand the available courses in the near future to provide additional educational resources for all PhD students. All of our activities are accessible to our members, including students working outside the OOA institutes ('buitenpromovendi'). 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. A great advantage of online courses is that PhD students who were working abroad could participate in our educational program.

For on-the-job training, OOA PhD candidates receive support from their supervisor/project leader, postdocs and technicians. Their research is embedded within more than 200 established research groups led by faculty members, many being prominent leaders in the scientific community with excellent track records in oncology research, as testified by their contributions to international scientific literature and conferences, memberships in scientific steering committees, and honorees of prestigious scientific grants and awards. These supervisors guarantee a superb environment for research and education in research. They are supported by the research skills, scientific knowledge and enthusiasm of staff members and promising junior investigators who help maintain high mentoring standards for our PhD candidates. Adequate supervision is an extremely important topic of interest and attention for OOA. In general, when embarking on a PhD track, the PhD candidate and the supervisor (promotor) will agree on a research plan, the PhD curriculum. The promotor is responsible for providing the PhD candidates with supervision, guidance and feedback. In most cases, a daily supervisor is appointed to continuously assess the progress of the PhD project and performance of the PhD candidate. Within Amsterdam UMC, various training courses are offered for both junior and senior supervisors.

# **Educational Programme**

In 2021, we organized 36 educational activities. Our professional knowledge courses focus on cutting-edge scientific topics and the core research activities at the associated institutes, covering specific tumor types and topics within oncology, as well as new groundbreaking technologies which will provide the students with the right skills and expertise to apply these methods in their own research. A subset of our courses is aimed at improving the 'general skills' of PhD candidates, which will not only help them successfully complete their PhD project, but also better prepare them for a future job. In 2021, we also implemented an extensive Ethics and Integrity in Science course and made it mandatory for all OOA PhD candidates. This course is designed to give early career PhD candidates a benchmark for values and ethical issues in scientific research, and also provides guidance to available resources and counselors in case issues of this nature arise in the future. Due to our focus on oncology and affiliation with cancer treatment centers, we highly value the translation of basic research findings into clinical applications, and vice versa. We therefore stimulate cooperation and integration of fundamental and clinical researchers.

The educational program designed by the OOA team is dynamic: evaluations of former courses, new developments in cancer research, and educational needs expressed by members all influence our course content and range. Our recurrent course program is supplemented by courses on currently relevant topics in oncology with the participation of acclaimed (inter)national scientists. Candidates make a selection from these courses according to their interest and background. Courses can take several days or up to two weeks. Upon completion, all participants receive a course certificate which includes the corresponding ECTS. The OOA education program not only teaches substantive knowledge, but also promotes cooperation and provides support, advice and inspiration.

Courses are typically given by senior faculty members, i.e. full professors, as well as associate- and assistant professors. Amsterdam UMC offers several training programs especially for lecturers including the 'Basiskwalificatie Onderwijs' and 'Senior Kwalificatie Onderwijs'. All OOA courses are evaluated by the participating candidates through an evaluation form. Comments are requested on the organization and content of the course and the performance of individual speakers. Course coordinators as well as the OOA team discuss these evaluations and take action accordingly.

Our OOA PhD candidates are allowed to join courses and educational activities organized by other (research) institutes and graduate schools as well. We closely collaborate with the Amsterdam UMC Doctoral School, AvL Academy, Medical Genetics Centre South-West Netherlands (MGC) and the Utrecht Graduate School of Life Sciences (CTO). These collaborations complement our educational program, allowing a better match with individual interests and needs of PhD candidates and expanding the opportunities to cooperate and interact. The OOA makes educational activities accessible to non-OOA PhD candidates when possible. Especially now that we have developed online courses, we are also allowing the enrollment of international non-OOA PhD candidates.

### **COURSE ORGANIZERS**

Leyla Azarang Roderick Beijersbergen Judy van Beijnum Jeroen Belien Maarten Bijlsma Piet Borst **Evelien Bos** Lenny Brocks Bram van den Broek Vincent Christoffels Suzanne Corsetto Amalie Dick Naomi Donner Zuhir Elkarghali Iris van t Erve Kyra de Goede Rodrigo Gomes Leite de Oliviera Nicole van Grieken Arjan Griffioen Karin van der Heijden Esmee Hoefsmit Else Huijbers Chavelli Kensen Patty Lagerweij Maartje Leemans Francisca van Leeuwen-Hilbers Elise Marseille Margarida Ferreira Martins Renee de Menezes Marjolein Mertz Nicole Nijhuis **Erik Reits** Hein te Riele Esther Ruhé Marianka Schmidt Jurgen Seppen Marcel Spaargaren Wendy Stam Bas van Steensel **Renaud Tissier** Rieneke van de Ven Anna van der Voort Nicole van der Wel **Rob Wolthuis** 

**36** Educational activities organized throughout 2021

765 Total number of course participants

4 1 Average evaluation rate of our courses (1 – 5 point scale)

Course organizers

**1.7** average credits per activity

# **Courses organized in 2021**



### 2x Basic Microscopy

### May 17 – 21, Sept 27 – Oct 1

This course covered the application of a range of imaging possibilities at Amsterdam UMC and NKI-AVL. They were presented in lectures, discussions and hands-on demonstrations. The individual research projects of the attending participants were discussed, allowing exchange of ideas with fellow participants and microscopy experts and operators.

Topics covered included: basic principles, specimen preparation and staining methods, quantitative analysis, electron microscopy.



### **Basic Oncology**

### June 21 - 25

This 5-day course provided a broad overview of oncology-related topics, with an emphasis on recent advances and issues that are relevant to the pathogenesis and treatment of cancer. The course was designed for all first/second year OOA PhD candidates, to provide them with a solid base in oncology already at an early stage of theirr PhD trajectory.



### October 25 - November 4

This two-week BioBusiness course focusses on both the theory and practice of entrepreneurship and business in the bioscience industry. The course consists of seminars given by a selection of top-notch speakers, and independent learning on the basis of exploring literature and business reports on selected topics.



### **CRISPR** genome editing

### March 16 – April 1

During this course participants will learn about the basic concepts of CRISPR-mediated genome editing, its experimental

design and a diverse range of CRISPR applications. Experts in the CRISPR field will present their work on different topics including large-scale screening, generation of *in vitro* and *in vivo* disease models, CRISPR diagnostics and therapeutic applications.

# 13x Ethics and Integrity – NKI edition

Each scientist sometimes faces dilemmas. While the extremes of the spectrum - falsifying and fabricating data and plagiarism are clearly very serious scientific misconducts, a wide range of research practices are in the "grey zone". We will address these our OOA course, issues in consisting of an interactive workshop, online module and discussion with supervisor.

# 4x Ethics and Integrity Amsterdam UMC edition

Each scientist sometimes faces dilemmas. While the extremes of the spectrum - falsifying and fabricating data and plagiarism are clearly very serious scientific misconducts, a wide range of research practices are in the "grey We will address these zone". our OOA course, issues in consisting of an interactive workshop, online module and discussion with supervisor.

# ★★★★↑ Genetic engineering in model organisms

### May 24 - 27

The course covered technology and applications of genetic engineering in basic and medical research. During four days, lectures given by experts in the field provided participants with an overview of the latest mouse genetic engineering and imaging technologies. Participants also attended the online seminar series

"11th Workshop on Innovative Mouse Models". Keynote speakers from leading laboratories present latest developments advanced genome alteration protocols, efforts to improve the relevance of disease models, including models for viral infection, and ethical issues related to animal experimentation. The course will be closed by meet-the-expert sessions with selected speakers



### Histopathology of Human Tumors April 15 - 16

Aim of this course is to give an introduction in the histology of malignant tumors and their precursor lesions. Microscopical structures, growth patterns, grading and staging systems, and different cell types present in selected tumor types will be explained and discussed by

# **★★★★☆**

pathologists.

### 4x How to write research papers

This course was designed to help to develop effective academic writing skills. We reviewed the principles of effective writing, examples of good and bad writing and tips for making the writing process easier. candidates worked improving academic writing skills through studying theory, performing analysis of published texts, and working on exercises. Moreover, they worked on writing, or revising, their own text, while receiving peer feedback and expert coaching.



### 2x ImageJ/Fiji

January 21 & 28, February 11 & 18 ImageJ is a public domain image processing and analysis program. The main objective of this course is to give the microscopy user a global understanding of the huge potential of the program. We went through all functionalities of the basic package and present specific

tools for use in (cell) biology. We also reviewed concepts and principles of image processing in general, in order to set a theoretical background.



### 2x Indesign thesis printing

#### Dec 3

Adobe InDesign is a desktop publishing software application for creating layouts. PhD students can use InDesign for creating their thesis. Nicole Nijhuis will gave an introductory workshop to InDesign.



# 2x Introduction to R for data analysis

### June 7, 8 & 10, Nov 8, 9 & 11

is an open-source, free environment for statistical and computing graphics. provides a large repository of statistical analysis methods, both classic and new. However, R has a steep learning curve. This course aimed at helping researchers climb this curve, enabling them to perform basic data analysis and graphic displays at the end of the course, as well as giving a platform from which they can deepen their R knowledge later on if necessary. Participants will also learn how to make dynamic reports, making their analysis transparent and reproducible.

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#### 2x Medical statistics with R

### October 5 - 9 -> ONLINE

In this course an introduction to basic statistical methods useful for biomedical data analysis was given. Concepts were taught in an intuitive manner, alternating between short lectures and practicals. This allowed for plenty of interaction and illustration with examples of practical interest. Participants who aimed to use more complex methods could use the concepts and skills learned during the course as basis, as the vast majority of statistical methods are implemented in R.



# Mouse morphology, genetics & function

#### **November 22 - 26**

Animal experiments, especially using mice and rats, are an important part of many PhD projects. Course participants were introduced into various aspects of research with rodents. The aim was to increase awareness of the physiology and genetics of experimental animals, thereby enabling better planning and execution of animal research.

The annual costs of the educational program and administrative costs are financed by Amsterdam UMC and NKI-AvL. In addition, the participating institutes provide administrative support. Thanks to the contributions of the participating institutes, all OOA PhD candidates can join our activities and courses free of charge.

Administrative support:

NKI-AvL: 0.80FTE administration

AUMC: 1.05FTE coordination &administration





# **Publications**

A total number of <u>101 theses</u> were defended throughout 2021 and <u>2300 peer reviewed papers</u> on oncology were published by AmsterdamUMC en/or NKI-AVL researchers. Five selected papers published by the OOA PhD students:

**Joris van de Haar** *et al.* Limited evolution of the actionable metastatic cancer genome under therapeutic pressure. Nature Medicine, 27(9), 1553-1563.

Claire Hoencamp *et al.* 3D genomics across the tree of life reveals condensin II as a determinant of architecture type. Science, 372(6545), 984-989.

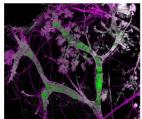
**Zowi Huinen** *et al.* Anti-angiogenic agents - overcoming tumour endothelial cell anergy and improving immunotherapy outcomes. <u>Nature Reviews Clinical Oncology</u>. Aug;18(8):527-540.

**Kevin Kos** (OOA Diamond PhD candidate) *et al.* Neutrophils create a fertile soil for metastasis. <u>Cancer Cell</u>, 39(3), 301-303.

**Sanne van Neerven** (OOA Diamond PhD candidate) *et al*. Apc-mutant cells act as supercompetitors in intestinal tumour initiation. Nature volume, 594, 436–441.

**Julien Vos** *et al.* I CARE study group 2021: Effect of general practitioner-led versus surgeon-led colon cancer survivorship care, with or without eHealth support, on quality of life (I CARE): an interim analysis of 1-year results of a randomised, controlled trial. <u>Lancet Oncology</u>, 22(8), 1175-1187.





**Med Net** 







**KUNT ER IETS AAN DOEN)** 

### OOA PhD students in the national media

Regularly, the media pays attention to research carried out by OOA-affiliated faculty, staff and PhD students. Articles and interviews appeared in the media. Highlights of PhD candidates included:

Colinda Scheele, de Volkskrant, January 2021

Daphne Huizing, January 2021

Vicky de Boer, MedNed, February 2021

Kelly Silverio Alonso - Duin, February 2021

Sanne van Neerven (OOA Diamond) Louis Vermeulen, June 2021

Bas Vaarwerk, de Volkskrant, November 2021





# **Talent Policy**

In 2013, NWO awarded OOA a grant of €800,000 to initiate the 'OOA Diamond Program'. This program allowed us to select and support four outstanding master's students with the ambition and talent to write and perform their own PhD research project. Currently, one PhD candidate has defended her thesis and the other three candidates are nearing completion of their PhD projects. As stated in Appendix 5, the four PhD candidates performed excellently with regard to publishing their scientific accomplishments and receiving grants and prizes. The OOA Diamond Program offered them many opportunities. A few of the candidates' quotes are: 'The Diamond Program opened many unimaginable doors for me to develop my career as a researcher', 'Apart from gaining the Diamond grant itself (which itself is an incredible head start for the career of an enthusiastic young scientists), the application process is very valuable, and allows applicants to become more skilled in grant writing, presenting and networking'. We have shown that the Diamond Program (i) keeps/attracts talented MSc students to work at one of our institutes (organization profit), (ii) leads to a more efficient MSc-PhD transition (process gain), (iii) leads to a feasible talent program (process and strategic profit), and (iv) lead to better integration of Master's and PhD programs run at the participating institutes. Given this success, it is our priority to continue the Diamond Program, however, financial support is to be secured.

Recently, the OOA started a pilot program with one of the Dutch WON (WetenschapsOrientatie Nederland) schools for pre-university (VWO) secondary education. WON schools offer an alternative learning pathway to students who are interested in scientific research. To advance the scientific orientation programs at WON schools, academics are needed to educate students about academic research in an accessible way. We organized a Masterclass given by two enthusiastic OOA PhD council members. This outreach provides meaningful opportunities to collaborate: the pre-university students are taught by OOA candidates (societal impact), simultaneously the OOA PhD candidates can share their knowledge and learn to "pitch" their research. The pilot was a great success. A few quotes: 'I thought it was very interesting that the PhD candidates talked about their own career and especially about their current research. It gave me a very clear picture'.

'At first it didn't seem interesting to do cancer research, but through this masterclass I realized that I really liked it more than expected'. Almost all of students indicated that the Masterclass gave them a better idea of what is involved in doing cancer research. Given this success, OOA is aiming to expand the introductory program to more secondary schools in the region.





# Onderzoekschool Oncologie Amsterdam Annual Report 2021

Text and design Dr. Esther Ruhé De Boelelaan 111 1081 HV Amsterdam

Email: <u>e.ruhe@amsterdamumc.nl</u>

www.ooa-graduateschool.org