ANNUAL REPORT 2022

Oncologie Onderzoekschool Amsterdam

- OOA -

Oncology Graduateschool Amsterdam




OOA INSTITUTES

Amsterdam UMC
Universitair Medische Centra

NETHERLANDS CANCER INSTITUTE
ANTONI VAN LEEUWENHOEK

UNIVERSITEIT VAN AMSTERDAM

VU VRIJE UNIVERSITEIT AMSTERDAM

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 2022

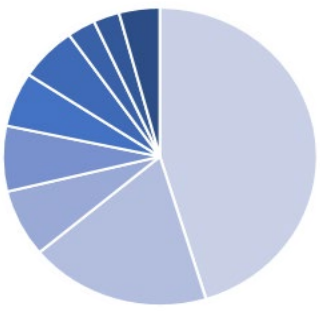
Click here for more details

26% international

36% male, 64% female

27% of projects funded by the participating institutes
15% by public funds
41% by research contracts
17% 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
- Neuroscience/Psychology/Sociology
- Other

From the executive team

It is essential that PhD candidates receive thorough and intensive guidance throughout their PhD program. The OOA organizes this through a training program and improving supervision. An attractive selection of courses is offered. Next to that, we pay attention to the personal well-being of students. For this, we have recently started a pilot with a course entitled 'How to positively influence yourself' given by former Olympic medal winner Edith Bos. The course is very well evaluated by the OOA PhD students. Several other levels of support and supervision are in place. Some support systems are organized by the institutes for all employees, including PhD candidates. Because the information was scattered on various websites and not easy to find, we recently created a summarizing OOA webpage.

One of the major hardships of the COVID-19 pandemic was the cancelling of the OOA retreats in 2020 and 2021. In 2022, there was finally a retreat again, though in a COVID-19-proof one-day event organized at the Cobra museum in Amstelveen. This great meeting was very positively evaluated for many reasons, not in the least because of the renewed social contacts with fellow PhD students.
An important note should be made about the PhD council. This is a group of PhD students from the different institutes that monitors the interests of students and functions as an advisory body for the executive team. The council has been very actively involved in organizing OOA events. We are very grateful to these council members.

Our registration system for PhD candidates has been improved extensively over recent years, largely thanks to improved cooperation with the administrators of the central ICT registration systems, like Hora Finita at location VUmc, and increased administrative support for the OOA. Our new ICT infrastructure enables PhD candidates to enroll online and track their progress.

We are confident that OOA will continue to improve in the future, making it an important home for the Amsterdam oncology-oriented PhD students!

On behalf of the OOA team,

Arjan Griffioen
OOA director
Chair

OOA TEAM

Executive team
Prof. dr. Arjan W. Griffioen
Chair, dean Amsterdam UMC (VUmc)

Prof. dr. Hein te Riele
Dean NKI-AVL

Dr. Marcel Spaargaren
Dean Amsterdam UMC (AMC)

Coordination
Dr. Esther M. Ruhé
Amsterdam UMC

Staff
Evelien Bos
Karin van der Heijden
Linda Kooter
Elise Marseille

PhD student council
Barbara Andrade Barbosa, Ben Ooms, Chavelli Kensen, Konstantina Strepi, Maud Schoot Uiterkamp

Advisory board
Prof. dr. Eric Eldering
Prof. dr. Jan Paul Medema
Amsterdam UMC

Prof. dr. René H. Medema
Prof. dr. Titia K. Sixma
NKI-AVL

Prof. dr. Chris J.L.M. Meijer
Prof. dr. Tom Würdinger
Amsterdam UMC

Faculty
OOA has over 200 faculty members. Click here for a list of all members.

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. structural biology. 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

To prepare PhD candidates for a successful career inside or outside academia, we aim to provide them all the same solid foundation. All OOA PhD candidates have to complete a uniform and mandatory training and supervision plan (TSP). This plan contains a number of mandatory activities, supplemented by education and activities that can be tailored to each candidate's own interest, background 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.

For on-the-job training, OOA PhD candidates receive support from their supervisor/project leader, post-docs 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 and NKI-AvL, various training courses are offered for both junior and senior supervisors.

Educational Programme

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'). In 2022, we organized 28 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. 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

Roderick Beijersbergen
Jeroen Belien
Maarten Bijlsma
Evelien Bos
Edith Bosch
Lenny Brocks
Bram van der Broek
Beatriz Carvalho
Noëlle Commandeur
Suzanne Corsetto
Amalie Dick
Donner
Remond Fijneman
Juan Garcia-Vallejo
Michael Glennon
Kyra de Goede
Nicole van Grieken
Arjan Griffioen
Esmee Hoefsmit
Karin van der Heijden
Chavelli Kensen
Patty Lagerweij
Maartje Leemans
Rordrigo Leite Olivera
Elise Marseille
Marjolijn Mertz
Arlene Oei
Erik Reits
Hein te Riele
Esther Ruhe
Martijn Smit
Marjanka Schmidt
Marcel Spaargaren
Wendy Stam
Bas van Steensel
Victor Thijssen
Rieneke van der Ven
Louis Vermeulen
Anna van de Voort
Nicole van der Wel

28 Educational activities organized throughout 2022

771 Total number of course participants

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

40 Course organizers

1.3 average credits per activity

Courses organized in 2022

Annual Retreat – 2.0 ECTS

May 13

This three-retreat focused entirely on research conducted by the PhD candidates themselves. Students not only presented their work, they were also in charge of chairing sessions and discussions. The retreat trained important skills and also provided an overview of research conducted within OOA at an early stage of the student's career, contributing significantly to the interaction between the students. The retreat is considered stimulating both scientifically as well as socially. In 2022, we organized a Covid-proof one-day event.

2x Basic Microscopy– 1.5 ECTS

May 16 – 20 and Oct 31 – Nov 4

This course taught the application of a range of imaging possibilities. They were presented in lectures, discussions and hands-on demonstrations. The individual research projects of the attending participants were discussed in relation to the demonstrated techniques, allowing exchange of ideas with fellow participants and microscopy experts and operators.

Basic Oncology – 2.0 ECTS

June 27 – July 1

This 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 their PhD trajectory.

2x Being Able To Influence Yourself Positively – 0.3 ECTS

April 13 and May 23

This workshop was organized for PhD candidates who experience stress or are in moments not happy and satisfied in doing their work. Participants were introduced in the I+/I- theory which are the two ways you can live your life from. They were helped to look at things differently, from a broader perspective and with ownership. They looked into stress and how to make it work for instead of against them. They worked with their own challenges and difficult situations and use them as a chance to become more self-aware, to find out what they really want and how to make that happen.

Career event

September 20

The NKI PhD council organized a successful local event where 9 OOA alumni presented their career track after finishing their PhD studies at the NKI-AvL. These pitches were followed by an informal pizza meeting enabling the PhD candidates to connect with the OOA alumni.

Colorectal Cancer – 1.5 ECTS

September 1 - 7

During this 5-day course, participants were introduced in the latest developments in colorectal cancer research and patient care. By interactive lectures given by scientists, through literature study and attending a symposium, all aspects of colorectal cancer were discussed, ranging from basic research to prevention, early detection and treatment of primary and metastatic cancer.

CRISPR basic course– 2.0 ECTS

April 4 -8

During this course, participants were introduced to basic concepts of CRISPR-mediated genome editing, and hands-on experimental design and protocols. In a series of short presentations and open discussion sessions, the program was focused on breaking down the steps needed to start using the most common CRISPR applications. On each day there were assignments to gain experience with the different tools available for CRISPR based technologies.

7x Ethics and Integrity in Science – 2.0 ECTS

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". These issues were addressed during this course including an overview of all available resources and counselors. The course consisted of three separate parts: an interactive workshop, an online module and writing an essay & discussing this essay with the supervisor.

Histopathology of Human Tumors – 0.6 ECTS

April 21 – 22

Aim of this course was 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 (based on preference of the participants) were explained and discussed by pathologists.

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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. PhD candidates worked on 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.

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ImageJ/Fiji - 0.6 ECTS

March 25 & Apr 1

ImageJ is a public domain image processing and analysis program. The main objective of this course was 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.

Immunophenotyping by Flow Cytometry – 1.5 ECT

November 7 -11

This course was aimed at PhD candidatesthat wish to expand their knowledge on the fundamentals of flow cytometry and multiplexed immunohisto-chemistry. participants learned the basic principles, how to design multicolor antibody panels, and obtain a comprehensive understanding of experimental design, necessary controls, data pre-processing, data QC, and traditional and high-dimensional data analysis strategies. Other topics included an overview of the most commonly used markers in immunophenotyping, the integration of immune-phenotyping strategies into immune monitoring studies, and successful data display in research articles and presentations.

Indesign thesis printing

July 11

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.

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3x Intervision Group – 1.0 ECTS

Intervision groups are small groups of professionals working in similar fields, who meet on a regular basis to gain insight into the problems they encounter at work. The participants try not to come up with solutions, but by asking questions, encourage the case provider to gain insight into his own case and how to take action on this. Important elements were to learn from the experience and ideas of colleague PhD candidates and to discuss problems without any hierarchical differences.

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Radiation Oncology – 1.5 ECTS

June20 - 24

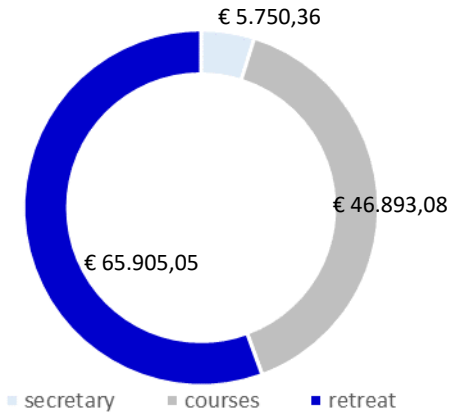
This course provided an overview of radiobiological and physical principles of radiation oncology, technical innovation in precision radiotherapy, and the route of the patient - via diagnosis, imaging and treatment planning – to therapy. Topics that were addressed: effects of irradiation on the DNA and cellular level, radiation response of tumors and normal tissues, physics of modern conformal radiotherapy, imaging, treatment planning and treatment of cancer patients with radiation alone or combined with chemotherapy or targeted therapy.

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

Amsterdam UMC:1.05FTE coordination & administration



Publications

A total number of 103 theses were defended throughout 2022 and more than 2200 peer reviewed papers on oncology were published by AmsterdamUMC and/or NKI-AVL researchers. Five selected papers published by the OOA PhD students are:

Maria Azkanaz *et. al.* Retrograde movements determine effective stem cell numbers in the intestine. **Nature**, 607(7919), 548.

Emilie Breekveldt *et al*. Colorectal cancer incidence, mortality, tumour characteristics, and treatment before and after introduction of the faecal immunochemical testing-based screening programme in the Netherlands: a population-based study. **Lancet Gastroenterology and Hepatology**, 7(1), 60-68.

Kim van Pul et al. Local delivery of low-dose anti-CTLA-4 to the melanoma lymphatic basin leads to systemic Treg reduction and effector T cell activation. **Science immunology**, vol. 7, no. 73, eabn8097.

Anne Spanjaart et al. Confused about Confusion, **New England journal of Medicine**, vol. 386, no. 1, pp. 80-87.

Sjors in 't Veld et al. Detection and localization of early- and late-stage cancers using platelet RNA, **Cancer Cell**, vol. 40, no. 9, pp. 999-1009.

Laurien Zeverijn *et al*. Harmonising patient-access programmes: the Dutch DRUG Access Protocol platform. **Lancet Oncology**, 23(2), 198-201.

OOA PhD students in the national media

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

Sjors in het Veldt, de Volkskrant, 1 september

Myriam Chalabi, Trouw, 12 september

Marcella Willemsen, MedicalFacts, 10 mei

Succes met bloedtest die kanker opspoort, nog wel vaak vals alarm

Ronald Veldhuizen
Amsterdam

Onderzoekers van het Amsterdam UMC melden succes met een test die vroegtijdig kanker in het bloed opspoort. Een felbegeerde techniek, want een vroeg ontdekte tumor is beter te behandelen. Critici vrezen overbehandeling en onnodige ongerustheid bij patiënten door vals alarm.

Het Nederlandse team, onder leiding van arts-onderzoeker Myron Best en hoogleraar Tom Würdinger, maakt voor de test gebruik van bloedplaatjes. Dat zijn manusjes-van-alles in menselijk bloed: ze helpen niet alleen bloed stollen en wondjes dichtplakken, maar zijn ook nauw verbonden met het afweersysteem.

Bijzonder belangrijk voor de test is dat bloedplaatjes hun vorm waarschijnlijk aanpassen op aanwezige tumoren, zegt Best. 'Ze vormen ook een schild rond kankercellen die de bloedbaan in gaan. We worden er steeds beter in om de verschillende gedaanten van die bloedplaatjes uit te lezen.'

Het diagnosewerk laat het team aan een computer over. Daarvoor verzamelden ze bloedmonsters van 236 patiënten met kanker, waaronder ook vergevorderde, herkent het programma terecht dat er een tumor aanwezig is. Als de kanker nog niet is uitgezaaid (tot en met stadium drie), werkt de test in ongeveer de helft van de gevallen.

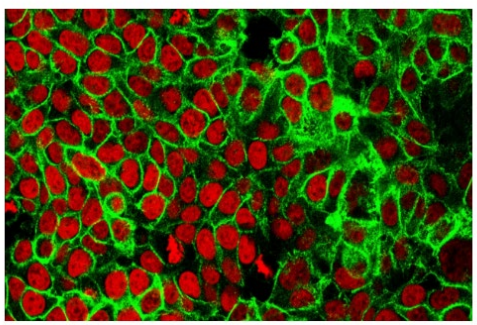
'Een keurige studie', zegt medisch statisticus Maarten van Smeden van het UMC Utrecht, die niet betrokken was bij het onderzoek en zelf veel werkt aan machinelearning. De onderzoekers laten volgens hem zien iets op het spoor te zijn. 'Het is een mooie beginstap.'

Valspositief

Voor massale kankerscreening is de test in de huidige toestand echter 'kansloos', schrijft hoogleraar klinische chemie Eleftherios Diamandis van de Universiteit van Toronto in een reactie. Dat komt doordat de computer nog relatief vaak onterecht veronderstelt dat een gezond persoon kanker heeft. Diamandis rekent voor dat van elke 100 mensen die met de test te horen krijgen dat ze kanker hebben, er bij 57 van hen geen sprake van een tumor is.

Door zoveel onzekerheid zouden jaarlijks duizenden Nederlanders onnodig extra medisch onderzoek moeten afwachten, dikwijls in spanning, om vervolgens te horen dat ze toch geen kanker hebben. Om die reden keurde de Gezondheidsraad enkele jaren geleden een verzoek af van het Erasmus MC om mannen uit te nodigen voor een bloedtest die prostaatkanker zou aanwijzen.

Onderzoeker In 't Veld erkent dat de test nog niet geschikt is om te gebruiken onder de brede bevolking. 'Om het aantal valspositieve uitslagen omlaag te krijgen, moeten we de computer ver-



Immuuntherapie succesvol bij een vorm van darmkanker

Vitiligo en melanoom: het fijne evenwicht tussen auto-immuniteit en ontsnapping aan de afweer

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