



With the summer holiday starting, please find the latest CRCG newsletter. We were very pleased with the recent announcement that multiple clinical and preclinical grant applications have been awarded by the Dutch Cancer Society. An excellent start of the summer! Congratulations to the successful applications: we are looking forward to exciting results...

Read the interviews with Bea Wisman (TARGON program) about cervical cancer screening and with Lara Barazzuol (DARE program) on the effects of irradiation on normal tissues.

Also, please check the recent PhD theses from CRCG, and our upcoming CRCG activities, including our annual PhD student meeting at 'Het Kasteel', with keynote speaker Prof. Christian Reinhardt (University of Cologne). In addition, we will organize new activities, to better connect within the CRCG (PI/postdoc BBQ in September), and with the community around us (societal outreach event in August).

For now: Enjoy the newsletter and the summer!

*Marcel van Vugt,
Director CRCG*



Funding Highlight: ZonMW 'Doelmatigheidsonderzoek' Grant Dr. Bea Wisman



One of the important funders of scientific research in the Netherlands is the Netherlands Organization of Scientific Research (NWO), which covers all aspects of science: from basic to clinical studies, from individual fellowships to consortium and infrastructure grants. For the medical sciences, funding is governed by the subdomain ZonMW.

In this issue, we interview Dr. Bea Wisman who recently received a ZonMW grant to investigate a new screening method to improve population-based screening of cervical cancer.

Bea Wisman recently received a ZonMW grant to perform a population-based study into whether a new and non-invasive method of screening for cervical cancer can be used to improve the screening protocols that are currently in place in the Netherlands. This grant is a collaboration between various departments of the UMCG (Pathology and Oncological Epidemiology) and two biotech companies (Abbott Molecular and CC Diagnostics).

A little bit of history... where did it start?

The topic of this grant has a long history for me and our research team. It started in the year 2003 when I, together with prof. dr. Ate van der Zee and prof. dr. Ed Schuurung, began investigating whether it was possible to identify (epi)genetic changes in cervical cancer and the benign earlier stages of this cancer, the so-called Cervical Intraepithelial Neoplasias (CIN). The ultimate goal of this work was to identify traits that could be used to diagnose this disease early. Over the next years of research, we made significant steps towards this goal, most notably the identification of a set of epigenetic markers that can be used to distinguish between healthy cervical tissue and premalignant CIN and cancerous tissue.

With these findings, we started the development of a PCR-based bioassay that is now being commercialized by a biotech company, CC Diagnostics. This bioassay makes use of cervical scraping material for the

CONTINUATION OF FUNDING HIGHLIGHT: ZONMW 'DOELMATIGHEIDSONDERZOEK' GRANT DR. BEA WISMAN

With this grant we thus hope to further improve the Dutch screening protocol for cervical cancer.

sensitive detection of cellular changes based on epigenetic profiling.

A little bit of background...what is cervical cancer and how is it screened for?

To understand the relevance of our work, it is important to know a bit about the pathogenesis of cervical cancer and how women are currently screened for cervical cancer. In brief, the hallmark pathogenic event for cervical cancer is the chronic infection with Human Papilloma Virus (HPV). This chronic HPV infection is the driver for malignant transformation. The current Dutch screening protocol for cervical cancer (for women in the age of 30-60) comprises testing for high risk HPV (hrHPV) infection with cytology as triage test on routine cervical scrapings collected during a general practitioner (GP) visit to screen for the presence of high-grade CIN and cervical cancer. Women also have the option to use a self-sampling device which is used at home and sent for testing to the laboratory. The self-samples are evaluated for the

presence of hrHPV, but if positive these samples cannot be evaluated with cytology. Therefore, in case of HPV positivity, women are invited to collect a cervical scraping by a GP to determine which women need referral for colposcopy.

However, there is an apparent barrier for many women to make this second step, leading to either women not getting the follow-up needed or entering follow-up at a later (too late) time. Consequently, not all women with cervical cancer or premalignant stages may be identified efficiently and timely. In addition, the fact that HPV infection is found at the time of the self-test, does not necessarily mean that these women are at risk. Therefore, many follow-up GP visits prove to be unnecessary, highlighting the need for better predictive testing.

The current grant...what is it about?

In the ZonMW grant awarded to me and my co-investigators prof. dr. Ed Schuurings and prof. dr. Truuske de Bock, we aim to validate this new screening method and to position this assay for future implementation in the standard Dutch screening protocol. Hereto, we will screen for epigenetic changes on the initial self-test material, sent by women for HPV testing, using panels of epigenetic markers developed both by academia and companies. This additional screening will be done alongside the regular screening in a large cohort of 2400 women and will

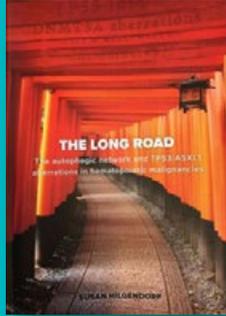
allow us to determine the sensitivity and specificity of this new diagnostic test. With this information, we will be able to conclude whether the addition of this new test can successfully diagnose those women in which HPV infection is accompanied by cellular changes, i.e. identification of high-grade CIN or cervical cancer. Herewith, only those women clearly at risk of developing cervical cancer would be rapidly identified for follow-up and further testing and GP visits of women not at risk can be avoided. With this grant we thus hope to further improve the Dutch screening protocol for cervical cancer.

> **Written by Edwin Bremer**

> **Photo provided by Bea Wisman**

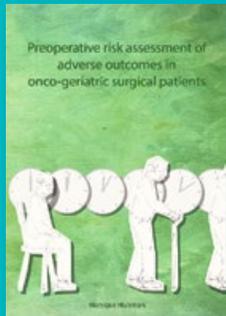
Dr. Bea Wisman obtained her PhD at the University of Groningen in the year 2000, with a focus on telomerase function in cancer. Following her graduation, she focused her efforts on defining genetic and epigenetic changes that underlie cancer development, with a special emphasis on cervical cancer. Her current research is focused on bringing her fundamental findings into clinical practice and reducing the burden of cervical cancer in society.

CRCG PhD thesis defences



The long road: the autophagic network and TP53/ASXL1 aberrations in hematopoietic malignancies

Ms. S. (Susan) Hilgendorf
July 2, 2018



Preoperative risk assessment of adverse outcomes in onco-geriatric surgical patients

Ms. M.G. (Monique) Huisman
July 4, 2018

Preclinical molecular imaging to study the biodistribution of antibody derivatives in oncology

Mr. J.F. (Jan) Warnders
July 4, 2018

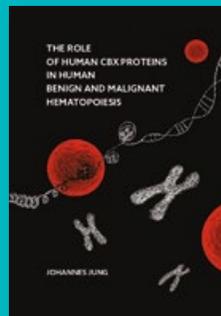


Referral patterns, prognostic models and treatment in soft tissue sarcomas

Ms. J.M. (Johanna) Seinen
September 10, 2018

Identifying aneuploidy-tolerating genes

Ms. J.E. (Judith) Simon
September 12, 2018



The role of human CBX proteins in human benign and malignant hematopoiesis

Mr. J.B. (Johannes) Jung
September 17, 2018



The role of reconstructive surgery in the treatment of soft tissue sarcomas

Ms. J. (Jelena) Slump
September 24, 2018

The use of organoids in the study of radiation response and therapeutic window

Mr. P.W.K. (Peter) Nagle
October 3, 2018

Localized extremity soft tissue sarcoma: towards a patient-tailored approach

Mr. M.G. (Marc) Stevenson
October 8, 2018

Hidden Markov models for the analysis of next-generation-sequencing data

Mr. A.S. (Aaron) Taudt
October 15, 2018

CONTINUATION OF CRCG PHD THESIS DEFENCES

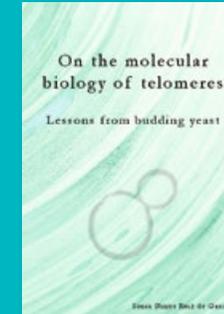
C/EBP β isoforms and the regulation of metabolism: a fine balance between health and disease

Mr. T. (Tobias) Ackermann
October 29, 2018



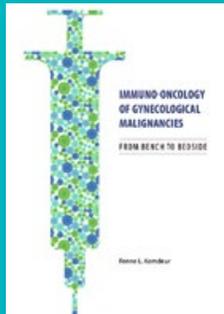
Disease-related malnutrition and nutritional assessment in clinical practice

Ms. L. (Lies) ter Beek
November 28, 2018



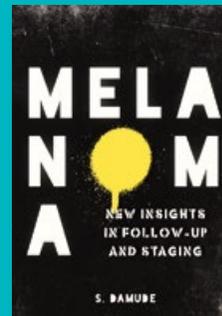
On the molecular biology of telomeres: Lessons from budding yeast

Ms. S. (Sonia) Stinus Ruiz de Gauna
December 3, 2018



Immuno-oncology of gynecological malignancies: From bench to bedside

Ms. F.L. (Fenne) Komdeur
November 21, 2018



Melanoma: New insights in follow-up & staging

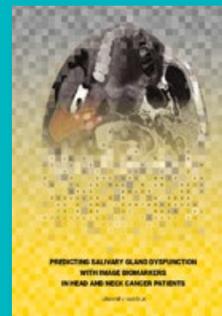
Ms. S. (Samantha) Damude
November 28, 2018

Targeting breast cancer cells and their microenvironment: Pre-clinical models and translational studies

Ms. H.H. (Hilje) Nienhuis
January 9, 2019

Testicular cancer: diagnostic and surgical strategies to improve outcome

Ms. C. (Cigdem) Ozturk
November 26, 2018



Predicting salivary gland dysfunction with image biomarkers in head and neck cancer patients

Ms. L.V. (Lisanne) van Dijk
November 28, 2018

Development of genetic manipulation tools in Macrostromum lignano for dissection of molecular mechanisms of regeneration

Mr. J.J. (Jakub) Wudarski
January 14, 2019

CONTINUATION OF CRCG PHD THESIS DEFENCES



Kinome directed target discovery and validation in unique ovarian clear cell carcinoma models

Mr. J.J. (Joseph) Caumanns
January 16, 2019

Clinical advances in musculoskeletal imaging: spondylodiscitis and pediatric oncology

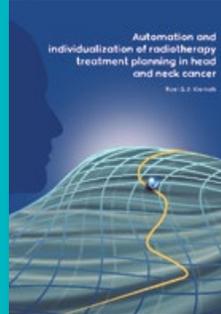
Mr. Ö. (Ömer) Kasalak
January 23, 2019

Preclinical evaluation and molecular imaging of HER family dynamics to guide cancer therapy

Mr. K.J.D. (Klaas) Kol
January 30, 2019

Risk-reducing surgery: Uptake & menopausal consequences

Ms. C.M.G. (Catheleine) van Driel
February 4, 2019



Automation and individualization of radiotherapy treatment planning in head and neck cancer patients

Mr. R.G.J. (Roel) Kierkels

February 6, 2019

MicroRNA expression and functional analysis in Hodgkin lymphoma

Ms. Y. (Ye) Yuan
February 13, 2019

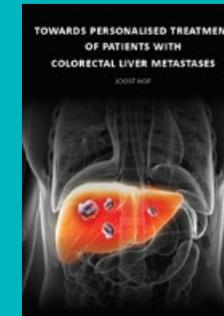
Neuroendocrine tumors; measures to improve treatment and supportive care

Ms. L.D. (Lotte) de Hosson
February 20, 2019



Survivorship care after testicular cancer: New insights in late effects of treatment and approaches to shared-care follow-up

Mr. H. (Hindrik) Boer
February 25, 2019



Towards personalised treatment of patients with colorectal liver metastases

Mr. J. (Joost) Hof
February 27, 2019

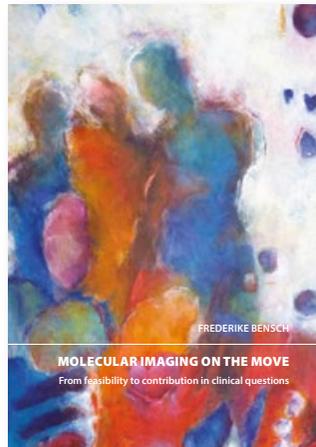
CONTINUATION OF CRCG PHD THESIS DEFENCES

Cum Laude

Molecular imaging on the move: From feasibility to contribution in clinical questions

Ms. F. (Frederike) Bensch

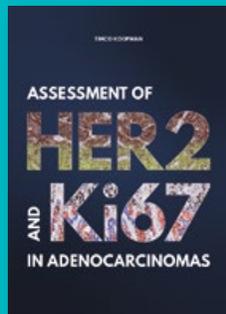
March 18, 2019



Autophagy in normal hematopoiesis and leukemia: Biological and therapeutic implications

Mr. H. (Hendrik) Folkerts

March 25, 2019



Assessment of HER2 and Ki67 in adenocarcinomas

Mr. T. (Timco) Koopman

April 3, 2019

Perfect pitstops: Towards evidence-based supportive care in children with cancer

Mr. E.A.H. (Erik) Loeffen

April 3, 2019

Assessment of malnutrition in patients with head and neck cancer: a multidimensional approach

Ms. M.J. (Martine) Sealy

April 10, 2019

Diagnostic strategies and surgical procedures for thoracic tumors

Mr. T.J. (Theodorus) Klinkenberg

May 1, 2019

Optimizing the treatment strategy of breast cancer

Mr. S. (Siqi) Qiu

May 1, 2019

Three dimensional virtual surgical planning for patient specific osteosynthesis and devices in oral and maxillofacial surgery. A new era.

Mr. J. (Joep) Kraeima

May 8, 2019

Genetic defects in myeloid malignancies and preleukemic conditions

Ms. G. (Gerbrig) Berger

May 22, 2019

Heterogeneity of cellular senescence and its implications for the development of markers

Ms. A. (Alejandra) Hernandez Segura

May 22, 2019

Replication-stress induced mitotic aberrancies in cancer biology

Mr. P.M. (Pepijn) Schoonen

May 22, 2019

Molecular mechanisms regulating epithelial-to-mesenchymal transition and therapy sensitivity in breast cancer and glioblastoma

Mr. Y. (Yuanke) Liang

June 18, 2019

Researcher in the spotlight: Dr. Lara Barazzuol, KWF Young Investigator and principal investigator



My name is Lara Barazzuol and I work in the UMCG both at the Department of Radiation Oncology and the Department of Biomedical Sciences of Cells & Systems, where I focus on identifying and finding ways to prevent radiotherapy-induced side effects particularly in the brain. I was born and raised in Italy. I earned my PhD in the United Kingdom at the University of Surrey in the field of radiation biology. I then held a postdoc position at the Genome Damage and Stability Centre at the University of Sussex. This is where I developed an interest in how the brain responds to DNA damage. I came to Groningen in 2016 when offered an amazing opportunity to join the research program here at the UMCG.

One year after arriving at the UMCG, I was awarded a Dutch Cancer Society Young Investigator grant (YIG) and a ZonMW Off-Road Award, which have allowed me to establish my own research group. Just last week I was awarded a 'Unique High-Risk grant' for a proposal that a colleague and I submitted to the Dutch Cancer Society last December.

CONTINUATION OF RESEARCHER IN THE SPOTLIGHT: LARA BARAZZUOL, PHD AND PRINCIPAL INVESTIGATOR

Can you describe the main problem you are trying to solve?

The focus of my research is to understand the underlying mechanisms influenced by radiotherapy treatment of patients with brain cancer. Most patients suffer from side effects due to damage to healthy brain tissue, including loss of neurocognitive function leading to a reduction in quality of life. The ultimate goal is to improve the quality of life of patients by developing novel therapeutic interventions and optimizing radiotherapy modalities for patients with primary brain cancers.

In collaboration with oncologists, my research aims to minimize damage using proton therapy (as part of my YIG grant). This is aided through work my group is performing in understanding the mechanisms of radiation-induced damage by using human brain

The focus of my research is to understand the underlying mechanisms influenced by radiotherapy treatment of patients with brain cancer.

organoids. The Unique High-Risk project that we were just awarded by the Dutch Cancer Society is actually focused on using brain organoids to measure the effect of radiotherapy on protein aggregation as a possible cause of neuronal damage. At the same time we are targeting this therapeutically, for instance by activating autophagy to promote degradation of protein aggregates, which can already partly be triggered by life-style changes (increased physical activity) but also by targeted drugs. Taking these aspects into account, my research encompasses in vitro mechanistic studies and, for a large part, animal studies to test the impact of radiotherapy on neurocognitive function.

What was your most joyful moment in research?

I have had many joyful moments in research making it difficult to choose just one. In 2017 I was awarded both a Young Investigator Grant and a ZonMW Off-Road Award. This finally meant that I could transition from a postdoc position into my role as a principal investigator to build my research team. The feeling that came to me during this move, which is a make-or-break point when pursuing a career in science, made me extremely happy. I take great joy these days as I establish my research and develop my group. Of course, the funding I received and the support of my colleagues was a major help giving me a sense of community.

You are more-and-more transitioning towards a supervisory role. Is your heart still in the lab or more in the steering/guiding?

I truly enjoy being in the lab! I sometimes find it is challenging to completely let go of the lab work and actually still prefer to work alongside my PhD students and technicians. With time, I expect that I will learn to let go more as I have excellent people working in my group.

What do you like most about doing science?

Every day there is a potential to learn or discover something that might make a difference to people. Lab work can be fun, especially when there is the possibility of using new techniques and biological systems to answer questions that have never been asked and answered before.

Is there anything 'boven' Groningen?

I like the research atmosphere here at the UMCG and in the CRCG, and the possibility to collaborate with clinicians/researchers that are close by. I also like my life in the Netherlands and especially the biking. I live in the city and it is great to be able to step on the bike and be in the lab quickly. I feel truly at home here. So no, nothing 'boven' Groningen...

> Written by Edwin Bremer

> Photo provided by Lara Barazzuol

Grants & Prizes

Several of the CRCG researchers have successfully obtained funding. Congratulations and we look forward to great science!

Dutch Cancer Society Research Projects

TITLE Treatment of radiation-induced hyposalivation with cell therapy (STOPXERO)
PROJECT LEADER Prof. Dr. Rob Coppes
 € 644,369

TITLE Androgen Deprivation therapy for Oligo-recurrent Prostate cancer in addition to radiotherapy (ADOPT)
PROJECT LEADER Dr. Shafak Aluwini
 € 899,591

TITLE GROINSS-V III: radiochemotherapy for patients with vulvar cancer with positive sentinel nodes
PROJECT LEADER Dr. Maaïke Oonk
 €388,466

TITLE A phase II study to determine the efficacy of therapeutic vaccine Vvax001 targeting HPV E6/E7 proteins
PROJECT LEADER Prof. Dr. Hans Nijman
 € 619,268

TITLE SONImage study: Can molecular imaging predict outcome to first-line endocrine treatment +/- CDK 4/6 inhibition in advanced ER+ breast cancer?
PROJECT LEADER Dr. Carolien Schroder
 € 597,603

TITLE Preclinical testing of prophylactic treatments for radiotherapy-induced cardiopulmonary complications (AVERT)
PROJECT LEADER Dr. Peter van Luijk
 € 587,615

TITLE Targeting protein aggregation to ameliorate radiotherapy-induced neurocognitive dysfunction
PROJECT LEADER Dr. Lara Barazzuol
 € 150,922

TITLE The role of the gut microbiota in early identification of hemato-oncological patients at risk for ICU-admission
PROJECT LEADER Dr. Walter van den Berg
 € 145,018

Agenda

KWF Roadshow

The aim of this meeting is to provide researchers with information on KWF's vision on its financing strategy for the coming years.

SPEAKERS

prof. Fred Valkenburg (KWF director) and KWF staff

DATE

Monday, November 4th, 2019, from 11.30-14.30

LOCATION

UMCG, Groningen

CCC / CRCG Outreach Day

The aim of the CCC/CRCG Outreach Day is to share the developments regarding scientific research, education and multidisciplinary collaborations at the UMCG with various disciplines outside the hospital. With the versatile program, CCC/CRCG hope to provide insight into technological developments in healthcare and the need for good multidisciplinary collaborations.

DATE

Thursday, August 29, 2019, from 13.00-16.30

LOCATION

UMCG, Groningen

7th Annual CRCG PhD Student Meeting

On Thursday, November 7, 2019, the CRCG organizes its 7th Annual PhD Student Meeting. This meeting is intended for all PhD students, MD/PhD students and their supervisors working in the research field of oncology. PhD students have to opportunity present their work through oral and poster presentations.

KEYNOTE LECTURE

prof. Christian Reinhardt (University of Cologne)

DATE

Thursday, November 7, 2019, approx. from 8.30-18.00

LOCATION

'Het Kasteel', Groningen



Colofon

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Michiel Hooiveld

Lay-out

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