ERIBA

European Research Institute for the Biology of Ageing

Report 2012 - 2016

university of groningen

University Medical Center Groningen

Report
2012 - 2016

ERIBA

www.eriba.umcg.nl

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Table of Contents

Foreword 6

1. Research 12

2. Principal Investigators 16
   - Eugene Berezikov
   - Cor Calkhoven
   - Michael Chang
   - Maria Colomé-Tatché
   - Gerald de Haan
   - Marco Demaria
   - Floris Foijer
   - Victor Guryev
   - Peter Lansdorp
   - Ellen Nollen
   - Katrin Paeschke
   - Judith Paridaen
   - Liesbeth Veenhoff

3. Research Collaborations 70
   - UMCG-RuG
   - Internationaal
   - Collaborations

4. Infrastructure and Key Expertise 92
   - UMCG Facilities
   - Fish Expertise
   - iPSC/CRISPR
   - Mouse Clinic
   - Seahorse XF96 Analyser Expertise
   - Single Cell Sequencing

5. Education 104

6. Business Development 110

7. Funding and Grants 114

8. Public Outreach and Dissemination 128

9. Facts & Figures 138
   - Staff
   - Funding
   - Publications
   - Awards
   - Invited Speakers

10. Governance and Management 174

11. Scientific Advisory Board 178

Sponsors

ERIBA,
the first five years

‘ERIBA investigators are basic scientists who explore diverse questions related to the biology of ageing. They collaborate with each other and with researchers and clinicians in- and outside the Netherlands.’

This report describes the accomplishments and future direction of the European Research Institute for the Biology of Ageing (ERIBA). Our research programs and progress are documented in the reports from the individual ERIBA researchers in the following pages. Here I want to acknowledge the organizations and people who have supported the successful launch of ERIBA and highlight some of our accomplishments. I also want to take this opportunity to make a few personal remarks as my five-year term as Scientific Director comes to a close.

Funding for ERIBA (€50 million) came from the Ministry of Economic Affairs, the Province of Groningen, the Collaboration of the Northern Netherlands, The European Union, the Noaber Foundation and the Pediatric Oncology Foundation Groningen. The planning for the building started in 2007. Uytenhaak architects put together a beautiful design for the building, which was constructed between 2010 and 2012 by Friso Bouwgroep. ERIBA officially opened its doors in November 2013. At the end of 2016 ERIBA employs 41 males and 51 females, including 13 group leaders. In the first five years a total of ~€27 million additional research funding was awarded to ERIBA scientists.

ERIBA investigators are basic scientists who explore diverse questions related to the biology of ageing. They collaborate with each other and with researchers and clinicians in- and outside the Netherlands. I hope that after reading this report you will agree that we have come a long way and that the road ahead has many opportunities for further development and transfer of knowledge. I fully expect that ERIBA will continue to impact on how we think about ageing for the knowledge-based “healthy ageing” strategies of the future.

From the onset, ERIBA has aimed to be transparent about the research that takes place within its doors. Transparency is necessary for any fundamental research organization not only to avoid being seen as an “ivory tower”, but also to expand the broad platform for the visionary direction of research in Groningen. Apart from a permanent exhibition on the ground floor of the ERIBA building, we communicate our research to the general public, students and professional colleagues in various other ways. For example, we organized a free online course for FutureLearn “Why do we age? The molecular mechanisms of ageing”. This course, put together by the University of Groningen and ERIBA researchers in 2015, has already run three times enrolling thousands of students, many of them in their retirement years! In 2015 we also organized an international meeting on “The Molecular Biology of Ageing”. This meeting attracted 300 researchers and students from around the world including many

of global research leaders.
The peer-reviewed funding and publications of our scientists are an indication of the quality of research in ERIBA. To ensure that we are on the right path we also receive advice from an independent scientific advisory board consisting of Jan Hoeijmakers (Chair, Erasmus University Rotterdam, the Netherlands), Johan Auwerx (EPF, Lausanne, Switzerland), Yves Barral (ETH, Zurich, Switzerland), Christine Mummery (University of Leiden, the Netherlands) and Helle Ulrich (IMB, Mainz). The ERIBA scientific advisory board meets every year to advise the Board of the UMCG about the quality and progress of science in ERIBA. We are immensely grateful to our scientific advisory board members and indeed all the individuals and organizations whose energy and support sustain us.

I want to also take this opportunity to make a few personal remarks. In 2009 Gerald de Haan asked me if I might be interested to direct a new research Institute focussed on the biology of ageing. I hesitated. After all, my wife and I had left the Netherlands in 1985 together with our young son to live and work in Vancouver, a spectacular city in a great country. Our daughter was born there, my research was going well and we had become Canadians. Why go back?

Apart from being flattered by the honour of being considered for the position, I was also intrigued by the challenge and attracted to the adventure. I was impressed with the vision of University President Sibrand Poppema and others of the University Medical Center Groningen (UMCG) to make "healthy ageing" a strategic direction well before this became trendy around a decade later. I knew Gerald from his work and he promised to work closely with me to deal with administrative and educational issues. His enthusiasm and the collegial atmosphere I encountered at all levels in the UMCG were very attractive. Further incentives were the impressive "LifeLines" project, the charm of the city of Groningen and the close proximity of the UMCG to the city center.

But a research Institute focussed on the biology of ageing? What should that look like? Why do we age and what determines lifespan? Those were and still are important questions with no obvious answers. Even genetically identical organisms such as yeast or worms show marked variation in lifespan under apparently identical conditions. We already know that socio-economic factors are very important predictors of human lifespan. However, a long lifespan also runs in families, suggesting the importance of heritable factors. No doubt ageing is a very complex process with environmental, genetic as well as "chance" components all weighing in. How could one hope to untangle such factors?

Since the mid 1990's my own research in the Terry Fox Laboratory at the BC Cancer Research Center in Vancouver had been focussed on the biology of blood-forming stem cells and the role of repetitive DNA at the end of chromosomes (telomeres) in stem cell divisions. Could the loss of telomeric DNA limit the number of times stem cells can divide? Could such a biological clock prevent tumor growth and cause ageing? Or do cells age because they acquire mutations over time as a result of imperfections in DNA replication and repair? These were questions I could take to Groningen!

I made no secret of my long held opinion that scientific progress is only possible when scientists are free to explore and engage in discussion with other scientists from vastly different fields. Creating the circumstances for talented scientists to explore and communicate with their peers is all you can do to stimulate progress and generate the new knowledge with its attractive spin-offs such as better prevention, better treatments and start-up companies that offer new products, measurements and tests. My appointment validated this approach so I set to work.
Together with Gerald de Haan we began recruiting ERIBA investigators. We agreed on selection criteria for candidates: curiosity, communication skills, a track-record of science related to ageing, some special technical skills and, perhaps most importantly, a desire to share knowledge and expertise with other ERIBA PI's. Application of these criteria resulted in an interesting mix of scientists as you can read in the following pages. I am very proud of helping bring together the current team of ERIBA scientists and help establish a climate of open communication that fosters excellence in research. Together with their team members ERIBA investigators represent a creative and dynamic force that will help us better understand why and how we age.

It has been a true pleasure and privilege to lead ERIBA for the first five years.

Peter Lansdorp
Scientific Director 2011-2016

'No doubt ageing is a very complex process with environmental, genetic as well as "chance" components all weighing in. How could one hope to untangle such factors?'

ERIBA,
the road ahead

As incoming Director, it is a pleasure and honour to share with you my ambitions for ERIBA.

We do not only wish to report on our accomplishments but also indicate where we would like to be five years from now.

ERIBA wants to excel at multiple levels. First and foremost, research at ERIBA will continue to provide novel, often unexpected, insight into the molecular and cellular mechanisms that cause ageing. In this report you will read a preview of where research in the ERIBA laboratories is headed, and in which fields we hope to make progress. We aim to pursue important questions and develop complete stories. This often implies that studies take considerable time to come to fruition, which is particularly true in the field of ageing research. Our philosophy to only publish discoveries when they are important and complete, is at times difficult to maintain in a landscape where researchers are expected to publish a specific number of papers each year, and where careers of doctoral students and postdoctoral fellows more often than not depend on publications in a selected number of journals.

Many agencies that fund research ask scientists to address questions that are of immediate use. I spent my summer holidays this year in beautiful Portugal, and visited Sagres, at the very South Western tip of Europe. While there, looking over the cliffs into the wide open ocean, I could imagine how in the Age of Discovery, scientists, sailors, merchants, and royalty must have asked each other "What is there on the other side?" They didn't know what they would find, but went ahead anyway. In the 21st century, discoveries are made in our own cells. We do not know what we will find, and nevertheless we want to proceed. Why? Because exploring uncharted territory is exciting and adventurous, and will reveal unknown treasures.

In the past five years, as ERIBA grew gradually with the arrival of new research teams to become what we are now, we have witnessed the start of multiple collaborations between these teams. Importantly, ERIBA researchers have also partnered with many clinical UMCG Departments, which we facilitated by awarding ten ERIBA seed funding grants. I strongly believe that some of the best science occurs as a result of what may seem to be an unusual combination of disciplines, approaches, and indeed personalities. It is my ambition to further support such collaborations, internally between ERIBA teams and 'externally' with UMCG/University of Groningen Departments.

In the upcoming five years, we will identify novel molecular mechanisms that could be targeted to delay, prevent, or reverse aspects of the ageing process. The detrimental effects of ageing become manifest in multiple tissues and are associated with numerous illnesses. Pharmaceutical companies typically focus their portfolio on targeting specific diseases, and have not put ageing research as a priority. However, in the last five years this perspective has changed and, excitingly, new industries which focus on developing strategies to delay aspects of the ageing process have emerged. We are thus starting to explore the possibility to work together with industrial partners to advance findings produced at ERIBA.

One of the greatest pleasures of a scientist is to witness students stepping out of the classroom into a laboratory to actually give a personal contribute to science themselves. ERIBA hosted and will continue to host a large number of students from all over the world. These students arrive at all levels, from high school students working on short science projects, to Bachelor and Master students working on their thesis, to Doctoral students on their way towards a Doctoral degree. ERIBA is keen to develop an educational track in ageing research, where students are embedded in an inspiring environment, surrounded by scientists from very different backgrounds. We will keep track of where ERIBA alumni go, and ensure that ERIBA is a great place to receive training, no matter whether students want to remain in academic or industrial science, in medicine, or in teaching.

We believe that it is important to share the findings generated in ERIBA with society at large. To this end we established the ERIBA Science Hall, both physically on the ground floor of the building, but also digitally at our website (http://www.eribasciencehall.nl). ERIBA has played a prominent role in many outreach activities in the last five years, as you can read in this report. The biological process of ageing, of which nobody escapes, intrigues people. ERIBA is expected to play an important role in providing our society with scientifically reliably knowledge on the truths and myths about ageing.

Looking back is easier than looking forward. We have come a long way, and established a world-class research Institute in a relatively short time, starting from scratch. In the next five years my ambition is to make ERIBA even better, and larger. Research in ERIBA will unravel novel and important mechanisms that contribute to ageing, and discover molecular and cellular intervention targets. ERIBA will be the place where students will find the best possible education in ageing research, to prepare them optimally for the next phase of their career. ERIBA will be one of the best research Institutes in the Netherlands, and a global leader in ageing research. The accomplishment of our aims is dependent on many variables, some of which are beyond our immediate control. Notably, our research remains very dependent on the funding climate, in the Netherlands and in Europe. Without exception, breakthroughs in biomedical science that are now considered standard care originate from findings made in basic biology. Only if we understand how ageing works, can we begin to explore how some of the deleterious aspects of the ageing process can be prevented.

I look forward to the next five years with great anticipation.

Gerald de Haan
Scientific Director 2016-

'In the 21st century, discoveries are made in our own cells. We do not know what we will find, and nevertheless we want to proceed. Why? Because exploring uncharted territory is exciting and adventurous, and will reveal unknown treasures.'

1. Research

1. Research

Our main mission is to understand what causes ageing. This may seem simple, but is actually enormously complex, because it is not trivial to define what ageing actually is. A specific molecular problem can cause ageing at multiple levels, in multiple tissues, and in multiple organisms. Therefore, ERIBA investigators address questions about ageing using collaborative, multi-disciplinary, technology-oriented approaches, employing multiple model systems. You will find a compilation of their major research accomplishments in this report, but we want to highlight a few examples to illustrate our philosophy.

Several scientists in ERIBA use unicellular yeast as a model organism. Yeast mother cells divide very frequently to produce daughter cells, but there is a limit to the number of daughter cells they can produce before they die. Using newly developed methods for culturing and data analysis, an accurate assessment was made showing how each yeast generation is different from the previous generation in molecular terms. It was found that ageing yeast cells have difficulties in safeguarding the composition of many protein complexes, suggesting that targeting protein synthesis could be used to interfere in the ageing process.

Other researchers in ERIBA use multicellular worms as model organisms. Some of these worm species, once adult, do not show any cell proliferation, whereas other species, in stark contrast, can regenerate a full body from a severed head. In worms in which no adult cell proliferation occurs, a dead cell cannot be replaced. Malfunctioning of cells, and cell death, can occur if proteins inappropriately aggregate, which is what happens in patients with Alzheimer's disease. ERIBA researchers are searching ways to intervene in protein aggregation, such that pathological protein plaques are delayed or prevented, and ageing is delayed.

It has long been known that caloric restriction extends health- and lifespan in many organisms. The molecular mechanism of caloric restriction has remained unclear, however. Researchers in ERIBA have generated a mouse in which a very small genetic change in a transcription factor that plays a key role in regulating metabolism mimics caloric restriction, without the mouse eating less. These mice are super healthy, lean, active, and protected from cancer. Efforts are under way to achieve the same result with a drug, instead of the genetic alteration. This study shows, once more, how pathways that contribute to ageing are extremely pleiotropic, but also suggest that targeting a single pathway could be beneficial for multiple tissues. Finally, researchers in ERIBA have successfully developed approaches in which genetic abnormalities can be detected in single cells, at very high resolution. This technology offers many opportunities to identify chromosomal instability in normal, ageing, and diseases tissues, study structural variation and haplotype differences between normal individuals and measure cellular heterogeneity in cancer tissues. These, and many other approaches in today's biomedical science, require the ability to integrate and interpret massively large data sets. Therefore, ERIBA researchers have developed multiple bioinformatic approaches to analyze genomic, transcriptomic, epigenomic and proteomic data, originating from all the various model systems that are used.

Please read about these developments, and much more in the next pages.

2. Principal Investigators

Eugene Berezikov
Group Leader of the Laboratory of Stem Cell Regulation and Mechanisms of Regeneration

‘Animals that can regenerate their body parts are powerful experimental models to study different aspects of stem cell biology.’

Biosketch

2012 – present
Junior full professor, ERIBA, UMCG, Groningen, The Netherlands

2007 – 2012
Group leader, Hubrecht Institute, Utrecht, The Netherlands

2001 – 2007
Postdoctoral fellow, Hubrecht Institute, Utrecht, The Netherlands
Postdoctoral fellow, Institute of Cytology and Genetics, Novosibirsk, Russia

Regeneration is the process of restoring lost or damaged tissues to their original state. The cellular basis for regeneration is provided by coordinated activity of stem cells, which give rise to various specialized cell types required to reconstitute a tissue. While humans and other mammals have only limited regeneration capacity, some other species can regenerate extremely well. For example, flatworms are often used as model organisms in research on regeneration because they can grow back entire body after amputation.

We aim to understand molecular mechanisms that regulate regeneration and activity of stem cells. For this, we are developing flatworms of the genus *Macrostomum* as experimental models. These animals have high regeneration capacity, are small, transparent, easy to culture, have short generation time and are amenable to genetic manipulation, making them attractive “laboratory-bench” models to study different aspects of stem cell biology.

We pioneered the development of the transgenesis method for *Macrostomum lignano* by demonstrating that microinjection of DNA constructs into eggs followed by low dose of irradiation frequently results in random integration of the transgene in the genome and its stable transmission through germline. To facilitate selection of promoter regions for transgenic reporters, we assembled and annotated the *M. lignano* genome, and showed its utility by generating multiple stable transgenic lines expressing fluorescent proteins under several tissue-specific promoters (Figure 1). The developed transgenesis method and annotated genome sequence will permit sophisticated genetic studies on stem cell biology in *M. lignano*.

We observed that repeated regeneration in *M. lignano* leads to extended lifespan, suggesting that it can be a suitable model to study the hypothesis of regeneration-induced rejuvenation. To test this hypothesis, we investigated phenotypical and gene expression changes during ageing and regeneration in *M. lignano*. We found that repeated regeneration of *M. lignano* causes a decrease in fitness, indicating that the regeneration capacity of the animal is not unlimited. At the same time, at the molecular level induced regeneration "rejuvenates" expression levels of several genes previously implicated in ageing, including Notch signaling pathway. These data suggest that *M. lignano* indeed can be a productive model to study molecular mechanisms underlying stem cell ageing and rejuvenation.

Future Directions

We will continue the development of the genetic and genomic toolbox for *Macrostomum*, focusing on transposon- and integrase-mediated transgenesis, genome manipulation by CRISPR/Cas9 system, and sequencing genomes of additional *Macrostomum* species. It is envisioned that comparative genomics studies will help dissecting flatworm-specific innovations responsible for the efficient regeneration in these animals. Furthermore, experiments on ageing in *Macrostomum* will be extended with the analysis of gene networks that sustain the animals under stress conditions. Finally, we started a new direction of research, exploiting the ability of *Macrostomum* species to cope with very high doses of ionizing radiation. Remarkably, these animals can survive more than 70 Gy of radiation and still produce viable progeny! For this to work, very efficient mechanisms of DNA damage response and stem cell protection musty be in place in *Macrostomum*, and dissecting these mechanisms might be informative for the development of DNA damage related therapies for prevention and treatment of cancer in human.

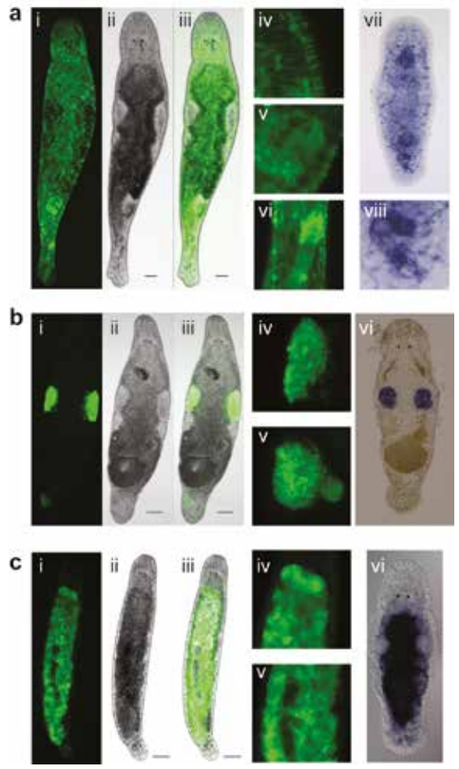

Figure 1. *M. lignano* tissue-specific promoter transgenic lines. (a) Muscle-specific MYH2::GFP reporter. (i) FITC; (ii) brightfield; (iii) merged; (iv-vi) detailed pictures: head, female opening, stylet; (vii-viii); Myh2 expression in whole animal and in stylet revealed by in situ hybridization. (b) Testes-specific ELAV4::GFP reporter. (i) FITC; (ii) brightfield; (iii) merged; (iv) detailed picture of testis; (v) detailed picture of the sperm filling the seminal vesicle; (iv) Elav4 expression in whole animal revealed by in situ hybridization. (c) Gut-specific APOB::GFO reporter. (i) FITC; (ii) brightfield; (iii) merged; (iv-v) detailed pictures; (vi) Apob expression in whole animal revealed by in situ hybridization. Scale bars are 100 μm.

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Junker JP, Noël ES, Guryev V, Peterson KA, Shah G, Huisken J, McMahon AP, **Berezikov E**, Bakkers J, van Oudenaarden A. (2014). Genome-wide RNA Tomography in the zebrafish embryo. Cell 159:662-75.

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Simanov D, Mellaart-Straver I, Sormacheva I, **Berezikov E.** (2012). The flatworm *Macrostomum lignano* is a powerful model organism for ion channel and stem cell research. (2012). Stem Cells Int. 2012:167265.

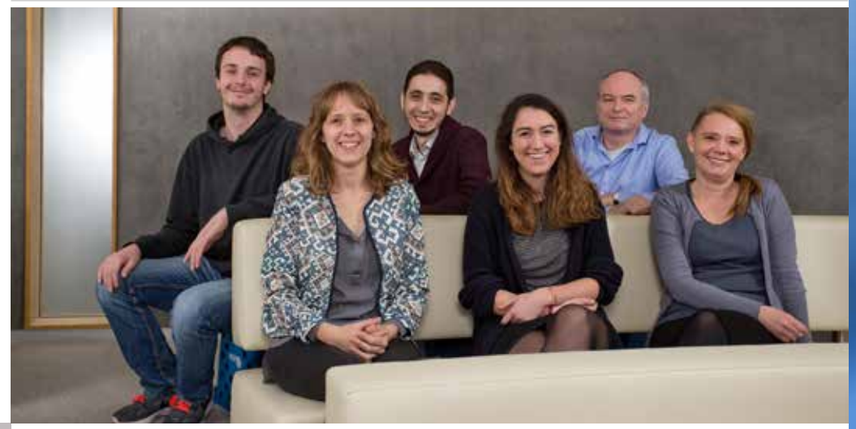
Berezikov E. (2011). Evolution of microRNA diversity and regulation in animals. Nat Rev Genet. 12:846-60.

GROUP MEMBERS

Ekaterina Ovchinnikova · Postdoctoral fellow
Frank Beltman · Technician
Jakub Wudarski · Doctoral student
Kirill Ustyantsev · Doctoral student
Lisa Glazenburg · Technician
Magda Grudniewska · Doctoral student
Margriet Grelling · Technician
Philipp Weissert · Postdoctoral fellow
Stijn Mouton · Postdoctoral fellow

Cor Calkhoven
Group Leader of the Laboratory of Gene Regulation in Ageing and Age-related Diseases

‘Understanding the molecular mechanisms of ageing will give us new insights in treatment of age-related diseases, including cancer.’



Biosketch

2013 –
Group leader / Professor of gene regulation in age-related diseases European Research Institute for the Biology of Ageing (ERIBA), University Medical Centre Groningen (UMCG), the Netherlands.

2005 – 2013
Group leader, Leibniz Institute on Ageing - Fritz Lipmann Institute (FLI), Jena, Germany.

2000 – 2005
Helmholtz fellow, Junior group leader, Max Delbrück Centre for Molecular Medicine (MDC), Berlin, Germany.

1998 – 2000
Postdoctoral fellow, Deutsche Forschungsgemeinschaft, Max Delbrück Centre for Molecular Medicine, Berlin, Germany.

1996 – 1998
Postdoctoral fellow, Marie Curie fellowship, Max Delbrück Centre for Molecular Medicine, Berlin, Germany.

Cellular factors that are involved in sensing nutrients and energy availability are decisively involved in ageing and lifespan determination, as well as in the development of age-related diseases like cancer and metabolic disorders. The research aim of our laboratory is to understand how the nutrient-sensitive mTORC1-pathway through the regulation of protein synthesis, controls the expression of specific sets of genes that alter the organism’s physiology, and contributes to the development of diseases. In addition, we investigate how mTORC1 itself is controlled in normal physiology and during the development of cancer.

Our laboratory is particular interested in the function of mRNA control elements, protein factors and microRNAs that are involved in mTORC1-controlled processes. We focus on translational (de-)regulation of C/EBPα and C/EBPβ transcription factors, which are key-regulators of metabolism, innate immunity and senescence. Recently

we showed that restriction of specific translation into the C/EBPβ-LIP protein isoform results in metabolic improvements in mice that resemble those found under calorie restriction, a dietary strategy that improves health and increases lifespan in most species. Mice that are genetically modified by removing the required uORF cis-regulatory element in the C/EBPβ mRNA have an improved metabolic and physical fitness, a reduced cancer incidence and an increased lifespan (Figure 2).

In another line of research we revealed a role of the proto-oncogene MYC in controlling mTORC1 through induction of the TORC1-inhibitor complex TSC1/2, which is required for cancer cell survival. This study showed that loss of TSC1/2 function leads to hyperactivation of mTORC1 and is synthetic lethal with oncogenic MYC through metabolic overloading and cell death. The results indicate that in certain cancer types loss of TSC1/2 function or hyperactivation of mTORC1 can be used therapeutically to kill cancer cells.

With the aim of 'translating' the fundamental research into clinical-pharmacological applications, we have developed reporter-systems for drug screening campaigns. With a unique high-throughput screening assay, aimed to identify compounds that reduce C/EBPβ-LIP expression, we successfully screened a small molecule library of known drugs. Indeed, we identified drugs with CR-mimetic properties that increased β-oxidation through down-regulation of LIP in cell culture.

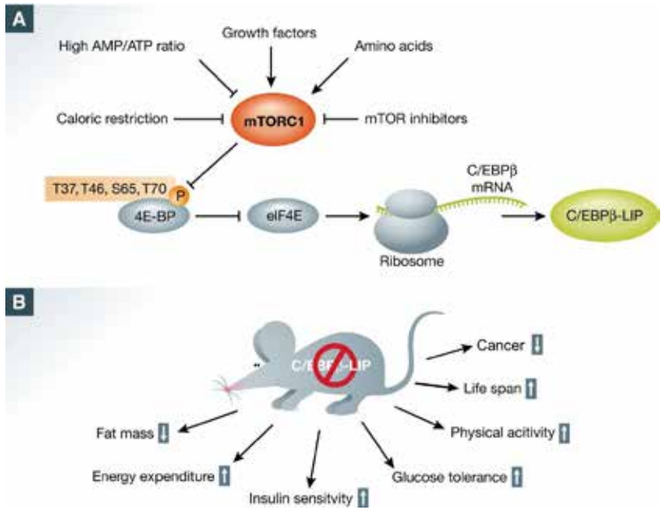


Figure 2. Adapted from News & Views related to Zidek et al (2015) by Albert and Hall (2015) EMBO Rep. 16, 881-882.A. The mTORC1 complex integrates nutrient- and energy availability with growth instruction signalling. Activated mTORC1 phosphorylates and inhibits 4E-BP causing release of the translation initiation factor eIF4E and stimulation of C/EBPβ-LIP translation. B. Mice that are deficient for C/EBPβ-LIP translation (C/EBPβΔuORF mice) display a variety of metabolic improvements, a reduced cancer incidence and an extended lifespan resembling wild-type mice under calorie restriction.

Future Directions

Our studies on the C/EBPβ-uORF-deficient mice have revealed that this mutation results in a reduced cancer incidence that is accompanied by lifespan extension. Preliminary studies with new mouse models that we generated (conditional C/EBPβ-LIP overexpression), as well as studies in cell culture, indicate that C/EBPβ regulation is involved in cancer progression, in particular in cancer. Therefore, future studies will focus on the oncogenic role of C/EBPβ-LIP in cancer development and its suitability as a tumour marker and/or therapeutic target. In addition, we will study the role of C/EBPα-microRNA regulatory networks and the role of post-translational modifications of C/EBPs in cancer development and metabolism.
A further research direction will focus on differential roles of the TSC1/2-mTORC1 axis in cancer progression and its suitability for therapeutic targeting. Finally, in collaboration with Fraunhofer IME ScreeningPort Hamburg we will setup small compound screening campaigns for the development of calorie restriction mimetic and anti-cancer drugs.

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Hartleben, H., Müller, C, Krämer, A., Schimmel, H., Zidek L.M., Dornblut, C., Winkler, R., Eichwald, S., Kortman, G., Kosan, C., Kluiver, J., Petersen, I., van den Berg, A., Wang, Z-Q and **Calkhoven, C.F.** (2016). Induction of TSC1 by deregulated MYC expression is required for cancer cell survival. in revision.

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Zidek, L. M., Ackermann, T. Hartleben, G., Eichwald, S., Kortman, G., Kiehntopf, M., Leutz, A., Sonenberg N., Wang, Z-Q, von Maltzahn, J., Müller, C., and **Calkhoven, C.F.** (2015) Deficiency in mTORC1-controlled C/EBPβ-mRNA translation improves metabolic health in mice. EMBO Rep. 16, 1022-1036.

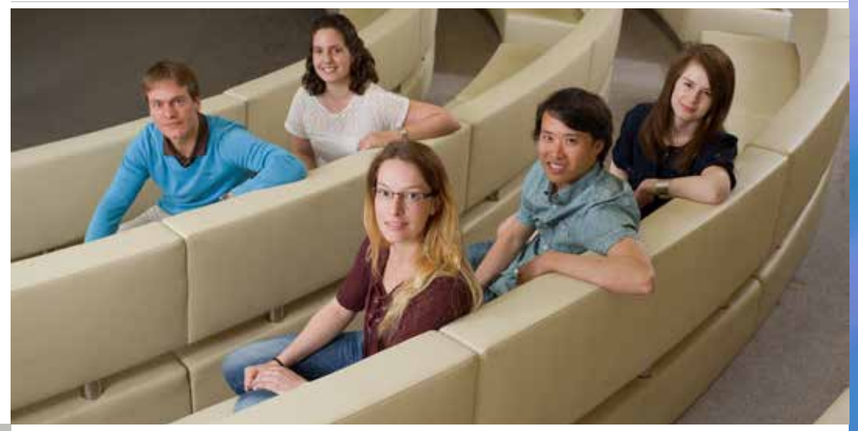
Dey S., Savant S., Teske B.F., Hatzoglou M., **Calkhoven C.F.** and Wek R.C. (2012) Transcriptional repression of ATF4 by C/EBPβ differentially regulates the integrated stress response. J. Biol. Chem. 287, 21936-21949.

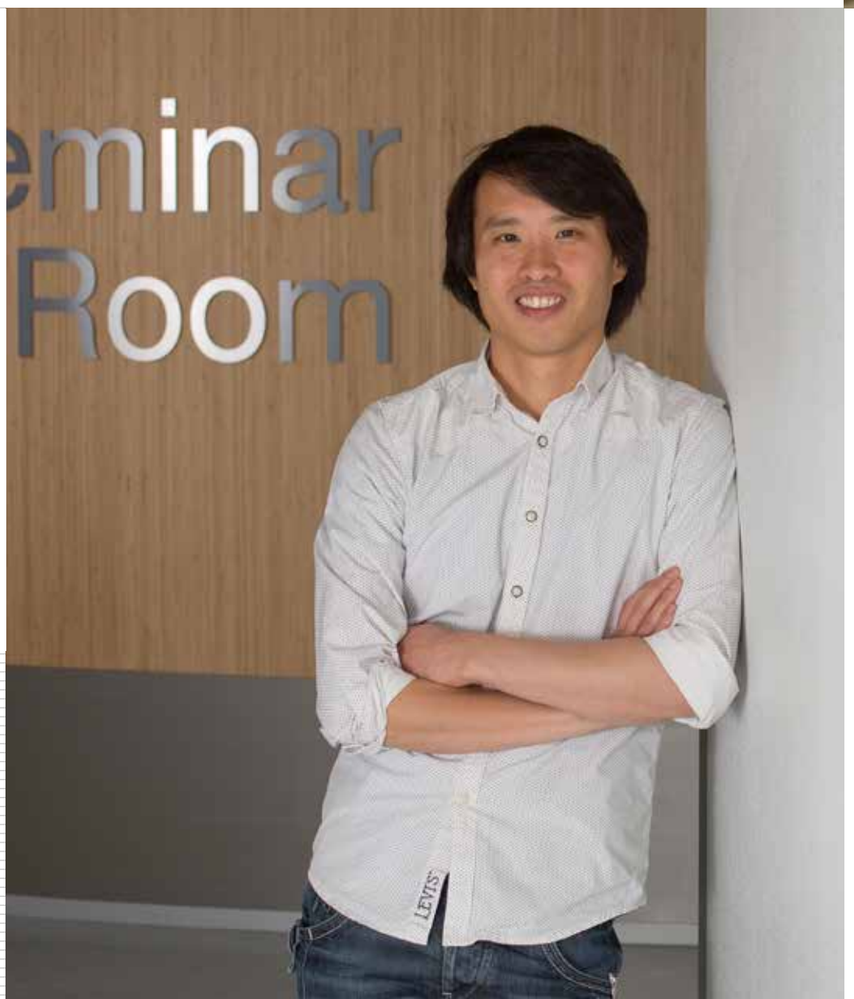
GROUP MEMBERS

Christine Müller · Research Associate
Tobias Ackermann · Doctoral student
Britt Sterken · Doctoral student
Amr Zaini · Doctoral student
Gertrud Kortman · Technician

Michael Chang
Group Leader of the Laboratory of Telomeres and Genome Integrity

‘The goal of our laboratory is to understand how cells protect their DNA from damage. Old cells and cancer cells are often unable to do so.’





Biosketch

2011 –
Assistant Professor, European Research Institute for the Biology of Ageing, University of Groningen, University Medical Center Groningen

2008 – 2011
Postdoctoral fellow in the Laboratory of Prof. Rodney Rothstein, Dept. of Genetics & Development, Columbia University, New York, USA

2006 – 2008
Postdoctoral fellow in the Laboratory of Prof. Joachim Lingner, Swiss Institute for Experimental Cancer Research, École Polytechnique Fédérale de Lausanne, Switzerland

2000 – 2005
Doctoral student., Department of Biochemistry, University of Toronto, Canada

The overall goal of our laboratory is to figure out the mechanisms used by a cell to protect its genome from becoming mutated or inappropriately altered or rearranged. The genome is duplicated in a process called DNA replication. If DNA becomes damaged, either as a consequence of normal cellular processes or due to exposure to DNA damaging agents, DNA repair pathways are employed to fix the damage. Defective DNA replication or DNA repair results in genome instability, which is a hallmark of both cancer and ageing.

Our laboratory studies these processes in the baker’s yeast *Saccharomyces cerevisiae*. Working with this unicellular organism has many experimental advantages. Yeast shares many of the same genes required for DNA replication and repair in humans, so insight obtained from yeast research can often be applied to humans as well.

We are particularly interested in understanding how homologous recombination (HR) is used to maintain genome integrity, both in general across the entire genome, and more specifically at regions located at the ends of chromosomes called telomeres (Figure 3). Telomeres help cells distinguish natural chromosome ends from double-strand DNA breaks (DSBs) in need of repair, and telomere shortening is associated with human ageing. HR is most commonly thought of as a pathway to repair DSBs, but we have recently found that HR is important to repair non-DSB damage, both genome-wide and at telomeres. For the former, together with Peter Lansdorp's group, we are measuring and mapping HR events genome-wide using single-cell sequencing. At telomeres, we have discovered that multiple HR subpathways are involved in repairing damage induced by telomere shortening. In addition, the laboratory performs high-throughput genome-wide screens to identify and characterize novel genes important for safeguarding genome and/or telomere integrity. Ongoing projects in the laboratory have identified genes important for an HR-mediated telomere maintenance mechanism, used in a subset of cancer cells, and genes important for suppressing the accumulation of mutations.

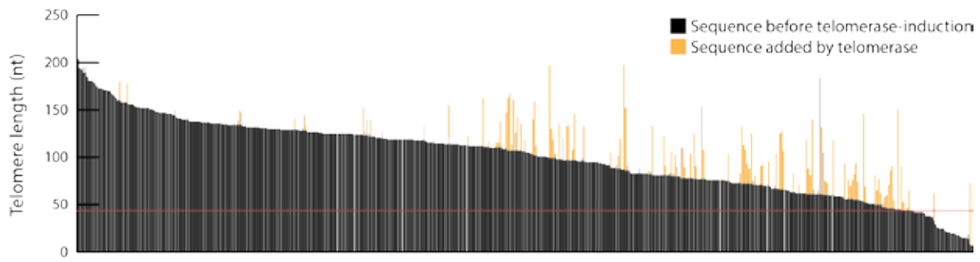


Figure 3. Telomeres are in part defined by specific DNA sequences. However, it is unclear how long a telomeric sequence needs to be for it to be recognized as a legitimate telomere. An ongoing project in the laboratory aims to address this question. This figure depicts the results of an experiment that tracks new sequences added by telomerase to telomeres of varying length. Each bar represents a sequenced telomere. The black portion of each bar represents telomere sequences before the induction of telomerase while the orange portion represents sequences added by telomerase. The telomeres are sorted based on the length of each sequence before telomerase-induction (from longest to shortest). Short telomeres, which are most in danger of becoming dysfunctional, are preferentially extended by telomerase, but extremely short telomeres are not. This finding defines a specific telomere length (red line) which demarcates a telomere from a DSB.

Future Directions

We will continue to study how cells protect their genome from the accumulation of mutations, chromosomal rearrangements, and telomere dysfunction. HR is a major DNA repair pathway important for proper genome maintenance. How HR is able to repair multiple forms of DNA damage, both genome-wide and specifically at telomeres, remains an area of active interest in the laboratory. In particular, we will pursue our observation that DSBs are not the most common lesions repaired by HR. We intend to determine what those lesions are and the proteins important for their repair. We will also investigate whether lack of repair of such lesions contributes to the acceleration of replicative senescence in cells lacking telomerase, the enzyme responsible for maintaining telomeres. Our ultimate goal is to determine how genome instability and telomere dysfunction promotes cancer and ageing.

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van Mourik, P.M., de Jong, J., Agpalo, D., Claussin, C., Rothstein, R., and **Chang, M.** (2016) Recombination-mediated telomere maintenance in *Saccharomyces cerevisiae* is not dependent on the Shu complex. PLOS ONE, 11(3): e0151314.

Gupta, A., Sharma, S., Reichenbach, P., Marjavaara, L., Nilsson, A.K., Lingner, J., Chabes, A., Rothstein, R., and **Chang, M.** (2013) Telomere length homeostasis responds to changes in intracellular dNTP pools. Genetics, 193(4): 1095-1105.

Chang, M.*, Dittmar, J.C., Rothstein, R. (2011) Long telomeres are preferentially extended during recombination-mediated telomere maintenance. Nat. Struct. Mol. Biol., 18(4): 451-456. *Corresponding author

GROUP MEMBERS

Clémence Claussin · Doctoral student
Daniele Novarina · Postdoctoral fellow
Paula van Mourik · Doctoral student
Sonia Stinus · Doctoral student

Maria Colomé-Tatché
Group Leader of the Laboratory of Quantitative Epigenetics

‘Understanding the epigenetic changes that occur during development, ageing and disease will help us modulate these processes to defer ageing and its associated diseases.’

Biosketch

2016 – present
Group Leader, Institute of Computational Biology, Helmholtz Zentrum München, Germany; AND Principal Investigator (PI) and Rosalind Franklin Fellow (10%FTE), European Research Institute for the Biology of Ageing, University Medical Center Groningen, University of Groningen, The Netherlands.

2013 – present
Principal Investigator (PI) and Rosalind Franklin Fellow, European Research Institute for the Biology of Ageing, University Medical Center Groningen, University of Groningen, The Netherlands.

2010 – 2013
Post-doctoral researcher in the group of Prof. Dr. R. C. Jansen, Groningen Bioinformatics Centre, University of Groningen, The Netherlands.

2009 – 2010
Post-doctoral researcher in the group of Prof. Dr. L. Santos, Theoretical Quantum Optics, Institute For Theoretical Physics, Leibniz University Hannover, Germany.

Our group is interested in understanding the epigenetic changes that take place during the processes of development, ageing and disease. The focus of the group is mainly on the role of DNA methylation and histone modifications. Epigenetic modifications contribute to the regulation of gene expression and this, at a genome-wide level, contributes to the determination of cellular identity.

For this reason, many relevant biological processes involve remodelling of the epigenome. This is the case during normal development, but epigenetic changes also take place during the development of many diseases, such as cancer, and a general deregulation of the epigenome has been observed in the process of ageing.

Understanding how the epigenome determines cellular identity requires genome-wide measurements of its molecular components, most notably DNA methylation and histone modifications. It has been possible to obtain such measurements with next generation sequencing using genetic material extracted from pools of millions of

cells. However, many important questions in biology require measurements of small cell numbers, or even single cells. This is the case in studies of early embryogenesis or in the analysis of cellular heterogeneity in tumors, for example. In the last few years new technologies have emerged that enable genome-wide measurements of DNA methylation and histone modifications in single cells and low inputs (few hundred cells) using also next generation sequencing.

In order to study genome-wide epigenetic changes, our group develops computational methods for the analysis of both bulk and single cell/low input epigenetic data, and we develop mathematical models to interpret it (Figure 4). Our goal is to develop computational methods that allow the study of different layers of the epigenome (i.e. DNA methylation and a set of histone modifications) across different time points (for example during ageing or development), cells or cell types, or conditions (cases versus controls). Then, using mathematical models we can correlate the detected epigenomic changes to changes on the phenotype (for example, gene expression) and can model epigenomic changes.

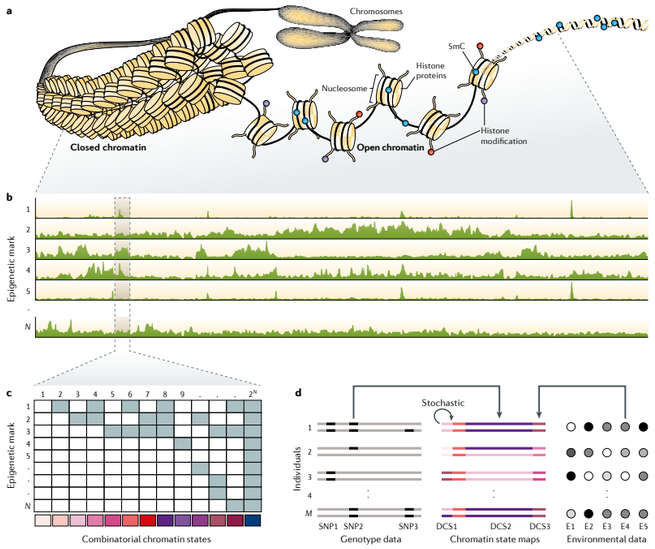

Figure 4. a) DNA is tightly packaged in cells and is functionally modified by a variety of epigenetic marks. b) The genome-wide distribution of different epigenetic marks can be measured using next-generation sequencing technologies. c) The computational challenge is to infer distinct chromatin states for each genomic position. These chromatin states are defined by the joint presence and absence patterns of the different epigenetic marks. The color code on the bottom denotes each unique state. This analysis leads to the construction of chromatin state maps. d) When comparing individuals the challenge is to determine differential regions between them in the chromatin states maps. These differential chromatin states (DCSs) can originate from DNA sequence polymorphisms, environmental factors or from stochastic changes.

Future Directions

We are currently working on the development of novel computational methods for the analysis and interpretation of single cell and low input epigenomic data. The methods will be embedded in a user-friendly computational pipeline in the common programming language R. The pipeline for single cell DNA methylation analysis uses single cell bisulfite sequencing data as input and calls DNA methylation states genome-wide. When data from several single cells is available the pipeline can be used to call regions of differential methylation in large populations of single cells. The pipeline for the analysis of histone modification data uses low input ChIP-seq data from multiple histone modifications as input and integrates these measurements into combinatorial chromatin states. When data from different samples is available (i.e. different treatments, tissues, etc.) the pipeline can also be used to call differential chromatin states between samples. Finally, the group works towards an integrated pipeline that will combine these two levels of epigenetic information (DNA methylation and histone modifications), and will integrate these results with other phenotypes.

SELECTED PUBLICATIONS

Genetic sources of population epigenomic variation. Taudt A, **Colomé-Tatché M**, Johannes F. Nat Rev Genet. 2016 Jun;17(6):319-32. doi: 10.1038/nrg.2016.45.

Rate, spectrum, and evolutionary dynamics of spontaneous epimutations. van der Graaf A, Wardenaar R, Neumann DA, Taudt A, Shaw RG, Jansen RC, Schmitz RJ, **Colomé-Tatché M**, Johannes F. Proc Natl Acad Sci U S A. 2015 May 26;112(21):6676-81. doi: 10.1073/pnas.1424254112.

Mapping the epigenetic basis of complex traits. Cortijo S, Wardenaar R, **Colomé-Tatché M**, Gilly A, Etcheverry M, Labadie K, Caillieux E, Hospital F, Aury JM, Wincker P, Roudier F, Jansen RC, Colot V, Johannes F. Science. 2014 Mar 7;343(6175):1145-8. doi: 10.1126/science.1248127.

Features of the Arabidopsis recombination landscape resulting from the combined loss of sequence variation and DNA methylation. **Colomé-Tatché M**, Cortijo S, Wardenaar R, Morgado L, Lahouze B, Sarazin A, Etcheverry M, Martin A, Feng S, Duvernois-Berthet E, Labadie K, Wincker P, Jacobsen SE, Jansen RC, Colot V, Johannes F. Proc Natl Acad Sci U S A. 2012 Oct 2;109(40):16240-5. doi: 10.1073/pnas.1212955109.

GROUP MEMBERS

Aron Taudt · Doctoral student

Gerald de Haan
Group Leader of the Laboratory of Ageing Biology and Stem Cells

‘If we understand how stem cells age, we can explore approaches to improve their functioning.’

Biosketch

2016 – present
Scientific Director of ERIBA, European Research Institute for the Biology of Ageing, University Medical Center Groningen, University of Groningen, NL

2014 – present
Dean Learning Community Molecular Medicine, Bachelor Program of Medical School University of Groningen

2011 – present
Group Leader of the Laboratory of Ageing Biology and Stem Cells, Scientific co-Director of European Research Institute for the Biology of Ageing, University Medical Center Groningen, University of Groningen, NL

2005 – present
Full Professor of Molecular Stem Cell Biology, Dept. Cell Biology, University Medical Center Groningen, University of Groningen, NL

1998 – 2005
Research Scientist/Associate Professor Department of Cell Biology, University of Groningen, NL

1995 – 1998
Post-doctoral fellow in the Laboratory of Prof. Dr. Gary van Zant, Blood and Marrow Transplant Program, Division of Hematology/Oncology, University of Kentucky, Lexington, KY, USA

The aim of studies our laboratory is to understand the mechanisms that specify normal hematopoietic stem cell functioning from birth to death. Blood cells have a limited lifespan, and are replenished constantly by bone marrow stem cells. Although this process is highly efficient, with age hematopoietic stem cells function worse, and this coincides with the incidence of various hematological diseases, including leukemia. Our laboratory is interested to find the cell-intrinsic mechanisms that contribute to loss of hematopoietic stem cell activity.

We have a particular interest in the role of epigenetic modifications in stem cell ageing. Polycomb Repressive Complexes (PRC) modify and read epigenetic marks on chromatin, and cause chromatin compaction or relaxation. A decade ago we discovered that overexpression of the PRC2 protein Ezh2 can prevent exhaustion of HSCs. More recently, we showed that the presence of PRC1 Cbx

proteins dictates whether HSCs selfrenew or rather differentiate, and thus serve as a toggle between these two fate choices.

HSCs from distinct inbred strains of mice display widely varying ageing characteristics. In an effort to determine the cause for these genetic differences, we have performed extensive genome-wide mRNA and microRNA expression analyses. In these screens we identified the microRNA125 family as candidate selfrenewing genes. Strikingly, miR-125 is able to induce transplantable stem cell activity in committed cells. This suggests that it is possible to reintroduce cellular potential in hematopoietic cells that have lost this potential.

We have developed tools that allowed us to label individual HSCs with a DNA barcode and follow the clonal progeny of labelled cells (Figure 5). This method has allowed us to determine clonal contributions of aged vs. young HSCs, but also the distributions of HSCs throughout the skeleton after transplantation. We showed at the clonal level that old stem cells produce fewer mature cells than their young counterparts.

Future Directions

We have identified several novel pathways that control HSC selfrenewal, which form the foundation of our future studies. We are keen to establish both downstream and upstream events of Polycomb and microRNA-controlled selfrenewal mechanisms, and will assess whether these pathways can potentially be manipulated pharmacologically. We will explore this in both mouse and human studies, as the mechanisms we have discovered appear to be evolutionary conserved. As selfrenewal is impeded during normal ageing, we will assess to what extent epigenetic and microRNA-controlled mechanisms of selfrenewal are affected during ageing.

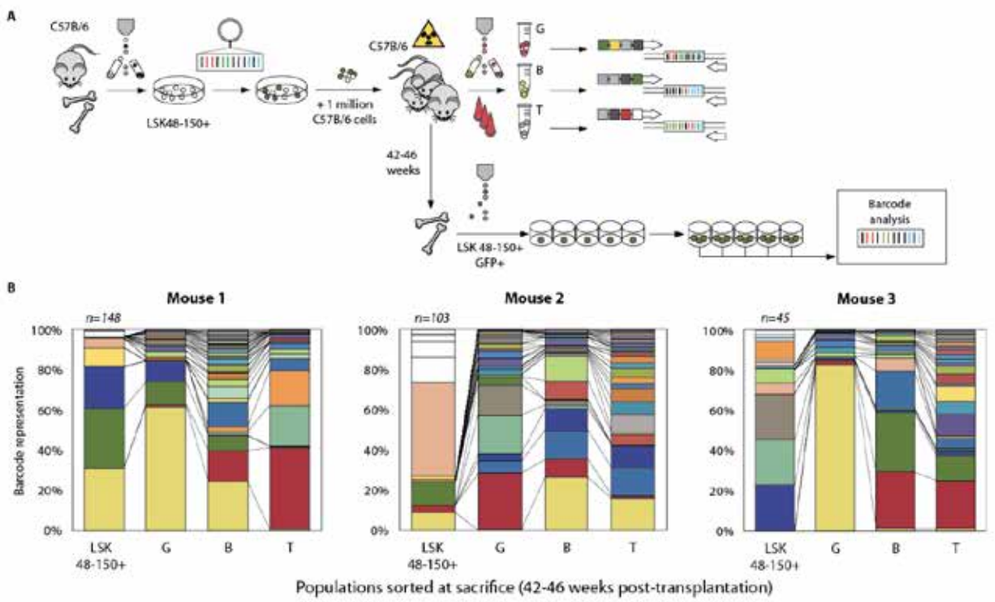

Figure 5. A. Experimental approach to DNA barcode purified hematopoietic stem cells to trace their clonal contribution to granulocytes, B-cells, T-cells and stem cells after transplantation. B. Clonal contribution in stem cells, granulocytes, and B- and T-cells in three mice, almost a year after transplantation. We detected deeply quiescent stem cells in bone marrow, that frequently do not contribute to active blood cell production

SELECTED PUBLICATIONS

Edyta E. Wojtowicz, Eric R. Lechman, Karin G. Hermans, Erwin M. Schoof, Erno Wienholds, Ruth Isserlin, Peter A. van Veelen, Mathilde J.C. Broekhuis, George. M.C. Janssen, Aaron Trotman-Grant, Stephanie M. Dobson2, Gabriella Krivdova, Jantje Elzinga, James Kennedy, Olga Gan, Ankit Sinha, Vladimir Ignatchenko, Thomas Kislinger, Ellen Weersing, Mir Farshid Alemdehy, Hans W.J. de Looper, Bader, GD, Martha Ritsema, Stefan J. Erkeland, Leonid V. Bystrykh, John E. Dick2 and **Gerald de Haan**. miR-125a Confers Multi-Lineage Long-Term Repopulating Stem Cell Activity to Murine and Human Hematopoietic Progenitors. Cell Stem Cell. 2016 Sep 1;19(3):383-96.

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Leonid V. Bystrykh, Evgenia Verovskaya, Erik Zwart, Mathilde Broekhuis, **Gerald de Haan**. (2012). Counting stem cells. Methodological constraints. Nat Methods. 2012 May 30;9(6):567-74.

GROUP MEMBERS

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Sabrina Jacobs · Technician
Erik Zwart · Bioinformatician
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Mirjam Belderbos · Postdoctoral fellow
Seka Lazare · Doctoral student
Alexander Bak Dinitzen · Doctoral student
Danielle Luinenburg · Doctoral student
Daozheng Yang · Doctoral student
Johannes Jung · Doctoral student

Marco Demaria
Group Leader of the Laboratory of Cellular Senescence and Age-related Pathologies

‘Cellular senescence is one of the basic mechanism of ageing, and represents an enormous therapeutic opportunity to extend healthspan’

Biosketch

2015 – present
Group Leader, Cellular Senescence and Age-Related Pathologies, ERIBA, UMCG, Groningen, NL

2011 – 2015
Post-doctoral fellow, Buck Institute for the Biology of Ageing, Novato CA, USA

2008 – 2011
Graduate student, Molecular Biotechnology Center, Torino, IT

Our group aims to understand the basic molecular and cellular mechanisms of ageing. In particular, the focus of the laboratory is on a specific cellular state, called ‘senescence’. Cellular senescence is a complex tumor-suppressive mechanism induced by many different stresses. Senescent cells irreversibly cease to proliferate, and are characterized by deep changes in morphology and gene expression. These changes are reflected by the secretion of inflammatory cytokines, proteases and other molecules that can alter the tissue microenvironment (a phenomenon termed the senescence-associated secretory phenotype, or SASP).

In recent years, we have developed new tools to identify, isolate and characterize senescent cells in mice and humans, and to study how senescent cells participate in several biological processes. Using these tools, we identified different beneficial and deleterious effects of cellular senescence, and we now aims at dissecting the various functions to develop new therapies for the

prevention of age-related diseases and cancer based on interfering with specific phenotypes of senescent cells. Of particular importance for cancer patients, we discovered that senescent cells are induced by different anti-cancer treatments, including radio- and chemotherapies. Using a newly developed transgenic mouse model (p16-3MR), we have been able to demonstrate that therapy-induced senescence (TIS) contributes to several side effects of anti-cancer interventions (Figure 6). Elimination of TIS cells is sufficient to improve healthspan by delaying and limiting different age-related dysfunctions. Moreover, the clearance of chemotherapy-induced senescent cells interferes with cancer progression and relapse. Interestingly, we observed in a clinical study performed in collaboration with the University of North Carolina at Chapel Hill that the level of fatigue cancer patients experience after chemotherapy treatment is directly correlated to the expression of senescence.

In recent years, targeting senescent cells has been shown to be an attractive strategy to delay the induction and/or progression of diseases associated with ageing. We contributed to understand the mechanisms by which senescent cells can survive, and found the importance of the anti-apoptotic machinery. We have found different interventions aimed at lowering SASP, which might also interfere with some of the deleterious effects of therapy- or age-induced senescent cells in vivoAgeing.

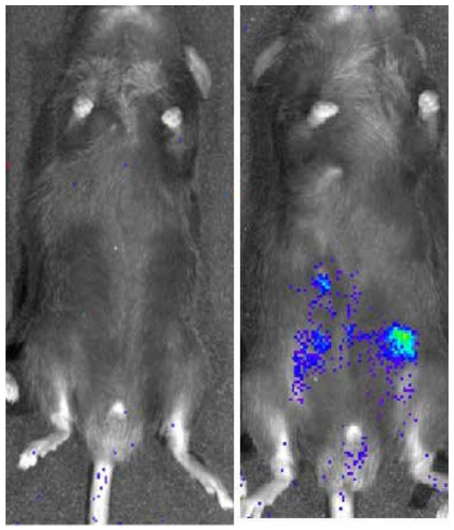

Figure 6. Senescent cells are induced in mice. Using a newly developed transgenic mouse model, we can identify the induction of senescent cells in mice with non-invasive techniques. The picture shows induction of senescence (visible by luminescence – blue/yellow dots) after treatment with chemotherapy (right mouse), compared to a non-treated mouse (left).

Future Directions

We now aim at understanding the molecular and cellular mechanisms that define the complex biological functions of senescent cells at the single cell level. In particular, we are interested to define the heterogeneity of the senescence phenotype, and how a senescent cell can cover beneficial or deleterious roles in a cell and tissue type-dependent fashion. We also try to understand whether the local or systemic environment can promote the accumulation of deleterious senescent cells. To reach this aim, new mouse models to dissect the contribution of senescent cells to different physiological and pathological functions, including cancer and age-related diseases, are currently under development. Dissecting the specific mechanisms by which senescent cells exert their functions in vivo will open the opportunity to design more potent and less toxic pharmaceutical interventions targeting only the deleterious side of the senescence phenotype.

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Demaria M*, O'Leary M, Chang J, Shao L, Liu S, Alimirah F, Koenig K, Le C, Mitin N, Deal AM, Alston S, Academia E, Kilmarx S, Valdovinos A, Wang B, de Bruin A, Kennedy BK, Melov S, Zhou D, Sharpless NE, Muss H and Campisi J. 2016. Cellular senescence promotes adverse effects to chemotherapy and cancer relapse. Cancer Discovery. DOI:10.1158/2159-8290.CD-ND2016-008. *corresponding author.

Christy B*, **Demaria M***, Campisi J, Huang J, Dodds SG, Williams C, Hubbard G, Livi CB, Gao X, Weintraub S, Curiel T, Sharp ZD, Hasty P. 2015. p53 and Rapamycin are additive. Oncotarget. 6:15802-15813. *these authors equally contributed.

Demaria M, Ohtani N, Youssef SA, Rodier F, Toussaint W, Mitchell JR, Laberge RM, Vijg J, Van Steeg H, Dollé M, Hoeijmakers J, deBruin A, Hara E, Campisi J. 2014. An essential role for senescent cells in optimal wound healing through secretion of PDGF-AA. Developmental Cell. 31:722-33.

GROUP MEMBERS

Alejandra Hernández Segura · Doctoral student
Boshi Wang · Doctoral student
Thijmen van Vliet · Doctoral student
Abel Soto-Gamez · Doctoral student
Simone Brandenburg · Technician

Floris Foijer
Group Leader of the Laboratory of Genomic Instability in Development and Disease

Biosketch

2011 – present
Junior group leader/ assistant professor European Research Institute for the Biology of Ageing, University Medical Center, University of Groningen, the Netherlands

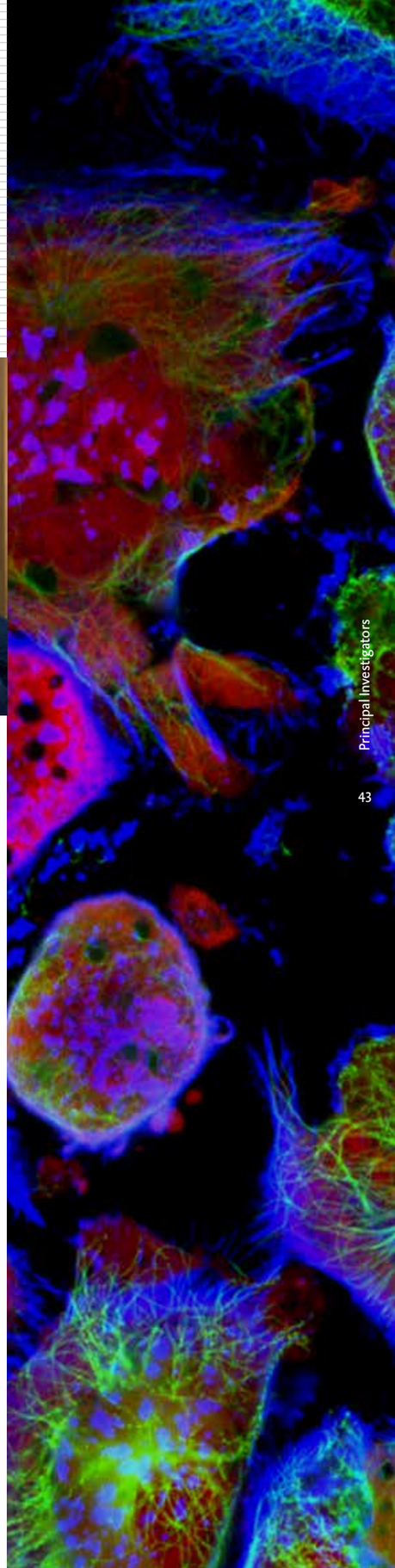
2009 – 2011
EMBO-funded postdoctoral fellow at Wellcome Trust Sanger Institute, Hinxton, UK (Allan Bradley lab)

2007 – 2009
Dutch Cancer Society-funded postdoctoral fellow at Harvard Medical School, Boston, USA (Peter Sorger lab)

2000 – 2006
Doctoral student at Netherlands Cancer Institute, Amsterdam, the Netherlands (Hein te Riele lab)

1995 – 2000
MSc and BSc student at Wageningen University (bioprocess engineering)

‘Understanding aneuploidy to improve cancer therapy.’



Aneuploidy, an abnormal DNA content, is a hallmark of cancer cells. Paradoxically, when provoked in an untransformed setting, aneuploidy reduces cellular fitness and proliferation potential, suggesting that aneuploid cancers have found ways to cope with the detrimental consequences of aneuploidy. Understanding such coping mechanisms will bring us closer to aneuploidy-targeting therapeutic strategies, the long-term aim of our lab.

To study the in vivo consequences of aneuploidy, we developed mouse models in which we can provoke aneuploidy in tissues of choice. We found that while aneuploidy alone is not sufficient to trigger cancer in the mouse, one predisposing hit (e.g. loss of p53), converts aneuploid cells into aneuploid cancer cells. The resulting animal model is allowing us to investigate the consequences of aneuploidy in a transformed and non-transformed setting. Using these models, we identified Prmt5 as commonly upregulated target in aneuploid lymphoma. We found that Prmt5 has an important role in

the activation of mTor signaling in aneuploid tumors, while it appears to have a another, more p-body-related role in untransformed aneuploid cells, which we are currently further exploring.

To test whether the tumors that arise in our models are indeed aneuploid and show a high grade of intratumour karyotype heterogeneity, we developed AneuFinder, a software tool to quantify karyotype heterogeneity in single cell sequencing datasets (single cell-sequencing platform developed by the Lansdorp lab) (Figure 7). AneuFinder analysis confirmed that the aneuploid tumors arising in our mouse models are highly heterogeneous as expected, and, importantly, that human aneuploid tumors exhibit different grades of karyotype heterogeneity, which we want to link to clinical outcome trough intervention studies in our mouse models as well as mapping karyotype heterogeneity in human tumors with a known outcome.

Future Directions

The long-term aim of the laboratory is identify intervention strategies that selectively kill aneuploid cells. For this we need to understand how chromosome missegregation impacts cancer which we will further map through single cell sequencing, and how cells respond to the resulting aneuploidy, both in an untransformed and in a malignant background. Genes that help aneuploid cells to adopt a more malignant fate are potential targets for cancer therapy. Making use of our finding that aneuploidy alone is not sufficient to trigger cancer in the mouse, we have setup genome-wide in vivo screens to identify genes and related biological pathways that convert aneuploid cells into cancer cells with promising results. By investigating the mechanisms behind these 'converter' genes, we expect to identify clinical targets that we can next validate using our mouse models for aneuploid cancer. In a parallel approach, we are following up on our recent finding that aneuploidy is tolerated by epidermal basal cells but not stem cells. Understanding which pathways trigger cell death of stem cells and survival of basal cells provides another strategy to identify pathways that trigger cell death in an aneuploid background. When we as such have identified candidate druggable pathways, we will validate our findings in vivo, making use of our recently developed mouse models in which we can monitor chromosome (mis-)segregation and the resulting aneuploidy by intravital imaging, allowing us to test candidate drugs in vivo.

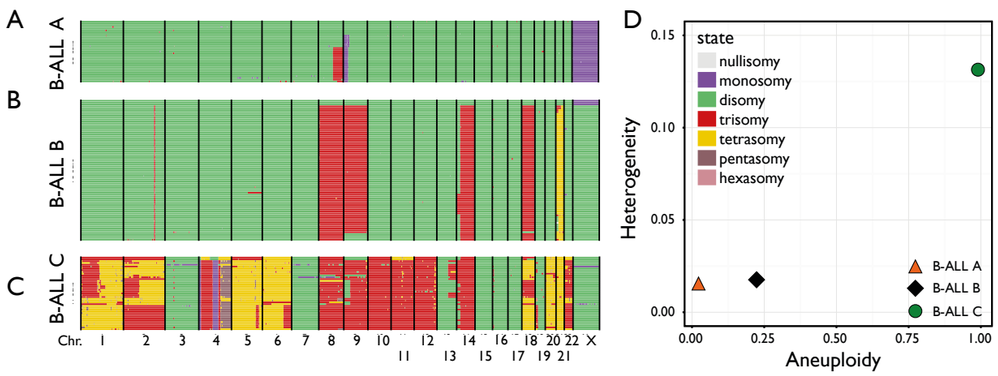


Figure 7. Quantification of intratumour heterogeneity in pediatric B-cell lymphoma using single cell sequencing. A-C) Single cell sequencing heat maps showing copy number variations of chromosome (fragments) for individual cells for three individual tumors (A-C). 30-46 cells were sequenced per tumor , colors (also see legend) represent copy number. Heats maps were plotted using AneuFinder. D) Intratumour heterogeneity (y-axis) and aneuploidy scores (x-axis) plotted for the three tumors analyzed in (A-C) showing that intratumour heterogeneities differ between patients.

SELECTED PUBLICATIONS

Bjorn Bakker*, Aaron S. Taudt*, Mirjam E. Belderbos, David Porubsky, Diana C.J. Spierings, Tristan V. de Jong, Nancy Halsema, Hinke G. Kazemier, Karina Hoekstra-Wakker, Allan Bradley, Eveline S.J.M. de Bont, Anke van den Berg, Victor Guryev, Peter M. Lansdorp, Maria Colomé-Tatché#| and **Floris Foijer#**. Single-cell sequencing reveals karyotype heterogeneity in murine and human malignancies. Genome Biol. 2016 May 31;17(1):116

Bakker B, van der Bos H, Lansdorp P.M. **Foijer F#**. How to count chromosomes in a cell: An overview of current and novel technologies. Bioessays. 2015 May;37(5):570-7.

Foijer F*#, Xie S.Z*., Simon J.E., Bakker P.L., Conte N, Davis S., Kregel E., Jonkers J, Bradley A and Sorger PK#. Induced chromosomal instability generates aggressive aneuploid lymphomas with a distinct transcriptional fingerprint. Proc Natl Acad Sci U S A. 2014 Sep 16;111(37):13427-32

Foijer F#, diTomasso T, Donati G, Hautaviita K, Xie SZ, Heath E, Watt FM, Smyth I, Sorger PK, and Bradley A, Spindle checkpoint deficiency is tolerated by murine epidermal cells but not hair follicle stem cells. Proc Natl Acad Sci U S A. 2013 Feb 19;110(8):2928-33

*Equal contributions; #corresponding author(s)

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Bjorn Bakker · Doctoral student
Judith Simon · Doctoral student
Klaske Schukken · Doctoral student
Laura Jilderda · Doctoral student
Lin Zhou · Doctoral student
Petra Bakker · Technician
Daniel Warmerdam · Senior Postdoctoral fellow IPSC/CRISPR facility
Stefan Juranek · Senior Postdoctoral fellow IPSC/CRISPR facility
Mathilde Broekhuis · Technician IPSC/CRISPR facility
Eslie Huizinga · Technician IPSC/CRISPR facility

Victor Guryev
Group Leader of the Genome Structure and Ageing

Biosketch

2012 – present
Team Leader, ERIBA, UMCG, Groningen, NL

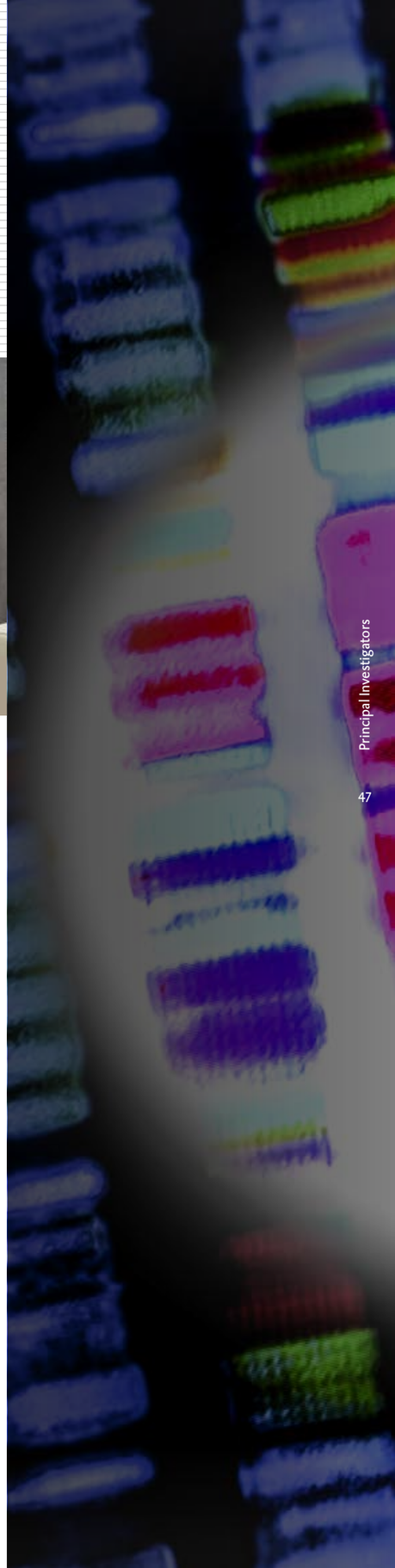
2007 – 2012
Head of Bioinformatics, Hubrecht Institute, UMCU, Utrecht, NL

2002 – 2007
Postdoctoral fellow, Genome Biology Group, Hubrecht Institute, UMCU, Utrecht, NL

'New multi-omics integrative approaches will help us to translate the trove of genomics data into factors driving molecular changes in cells and organisms. This step is of primary importance for emerging personalized medicine.'

Research in our group is aimed at understanding structural changes in human genomes. These changes may differentially affect health and disease predisposition in different individuals, be introduced during the ageing process, or result from cancer-related genome instability. Knowing the mechanisms that influence structure and functioning of our genomes is important for better understanding of genetic and environmental risks as well as for disease prevention. Recent studies highlighted the multitude of effectors and mechanisms that play key roles in protecting our genomes from structural alterations.

Heritable defects in DNA repair pathways are known to underlie many severe diseases that are associated with progeria, including Bloom syndrome, Cockayne syndrome and many others. Intriguingly, whole genome studies of mutations that originated during the last generation indicate a marked heterogeneity of de novo mutation rates



within the general population (e.g. a healthy cohort of 250 Dutch families studied by Genome of the Netherlands, GoNL). Individuals within populations are characterized by very different amounts of acquired de novo mutations. These individual-specific mutation loads are incompatible with random mutation spread and indicate that cells of some subjects are less efficient in maintaining their DNA error-free. With current progress in the field of genomics and prospective plans to decipher genomes of million(s) of people, we can expect substantial advances in out knowledge about personal mutation loads.

To learn more about inter-individual changes in human genomes we employed data from one of the pioneering project to characterize genomes of a general population. Genome of the Netherlands (GoNL) project represents an open collaboration among number of Dutch and international groups aimed at better understanding genome build-up and diversity in 250 healthy families. Focusing on structural changes, we characterized the load, distribution, inheritance and functional consequences of large segmental changes in a general population (1). A large part of structural variation is contributed by activity of mobile elements in our genomes (Figure 8) that might be important players in disease etiology. We also reported a way to impute SVs offering a practical way for inclusion of structural variants in association and other study types.

The team has developed several methods to characterize structural genome changes that are present in modern human population, de novo mutations originated in last generation and somatic mutations that are present in sub-population of cells. We also involve other data modalities by analysis of transcriptomes and proteomes from the same individuals to investigate the distribution and functional effects of these changes.

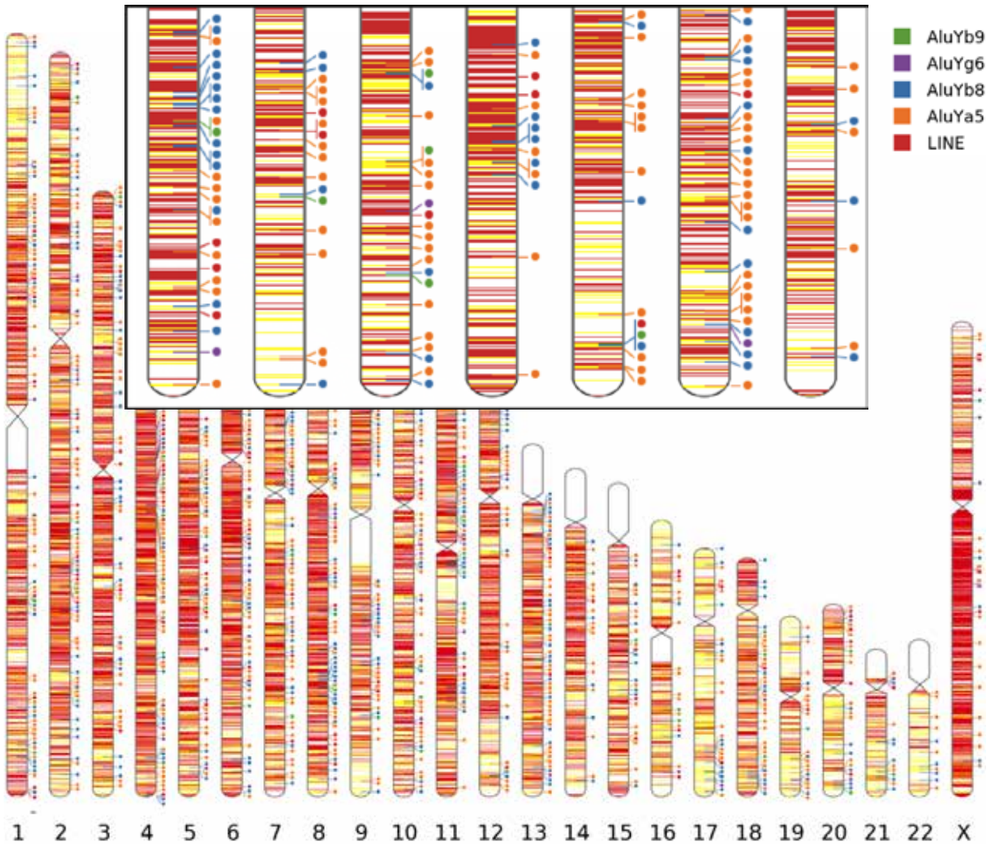


Figure 8. Dynamics of new insertions of SINE and LINE retratransposable elements in genomes of 250 Dutch families. Distribution of known retrotransposon locations is shown along the chromosomes (SINEs in yellow, LINEs in red). Newly discovered retrotransposon insertions are given in circles. Four recently emerged elements belonging to AluY family exhibit a very high retrotransposition activity and might be a major source of disease-related mutations. Inset: zoom-in on parts of chromosomes 9-14 showing non-uniform distribution of SINE/LINE integrations revealing genomic cold- and hotspots.

Future Directions

With current progress in the field of genomics and prospective plans to decipher genomes of million(s) of people, our knowledge about personal mutation load will increase dramatically. Our group will continue to investigate the molecular changes in genome structure and their function during the ageing process. We aim to develop new methods of detection and quantification and functional characterization of somatic point and structural mutations using genomics, transcriptomics and proteomics data. Next to that we will explore the nature and genome-wide patterns of mutation occurrence that will shed the light on the key processes responsible in generation of somatic genome alterations. The overall aim of the research is to better understand inherent and environment-associated alteration in DNA structure, composition and function.

SELECTED PUBLICATIONS

Hehir-Kwa JY, Marschall T, Kloosterman WP, Francioli LC, Baaijens JA, Dijkstra LJ, Abdellaoui A, Koval V, Thung DT, Wardenaar R, Renkens I, Coe BP, Deelen P, de Ligt J, Lameijer EW, van Dijk F, Hormozdiari F, The Genome of the Netherlands Consortium, Uitterlinden AG, van Duijn CM, Eichler EE, de Bakker PIW, Swertz MA, Wijmenga C, van Ommen GB, Slagboom PE, Boomsma DI, Schönhuth A, Ye K, **Guryev V.** (2016) A high-quality human reference panel reveals the complexity and distribution of genomic structural variants. Nature Comm. 7, 12989.

Kloosterman WP, Francioli LC, Hormozdiari F, Marschall T, Hehir-Kwa JY, Abdellaoui A, Lameijer EW, Moed MH, Koval V, Renkens I, van Roosmalen MJ, Arp P, Karssen LC, Coe BP, Handsaker RE, Suchiman ED, Cuppen E, Thung DT, McVey M, Wendl MC; Genome of Netherlands Consortium, Uitterlinden A, van Duijn CM, Swertz MA, Wijmenga C, van Ommen GB, Slagboom PE, Boomsma DI, Schönhuth A, Eichler EE, de Bakker PI, Ye K, **Guryev V.** (2015) Characteristics of de novo structural changes in the human genome. Genome Res. 25, 792-801.

Low TY, van Heesch S, van den Toorn H, Giansanti P, Cristobal A, Toonen P, Schafer S, Hübner N, van Breukelen B, Mohammed S, Cuppen E, Heck AJ, **Guryev V.** (2013) Quantitative and qualitative proteome characteristics extracted from in-depth integrated genomics and proteomics analysis. Cell Rep. 5, 1469-78.

van Heesch S, Mokry M, Boskova V, Junker W, Mehon R, Toonen P, de Bruijn E, Shull JD, Aitman TJ, Cuppen E, **Guryev V.** (2013) Systematic biases in DNA copy number originate from isolation procedures. Genome Biol. 14, R33.

GROUP MEMBERS

Tristan de Jong · Doctoral student
Victor Bernal · Doctoral student

Peter Lansdorp
Group Leader of the Genetic Instability and Ageing Center

‘No doubt ageing reflects complex biological processes that interact at multiple levels. Collecting accurate information about cells as they age is a first step to better understand ageing’

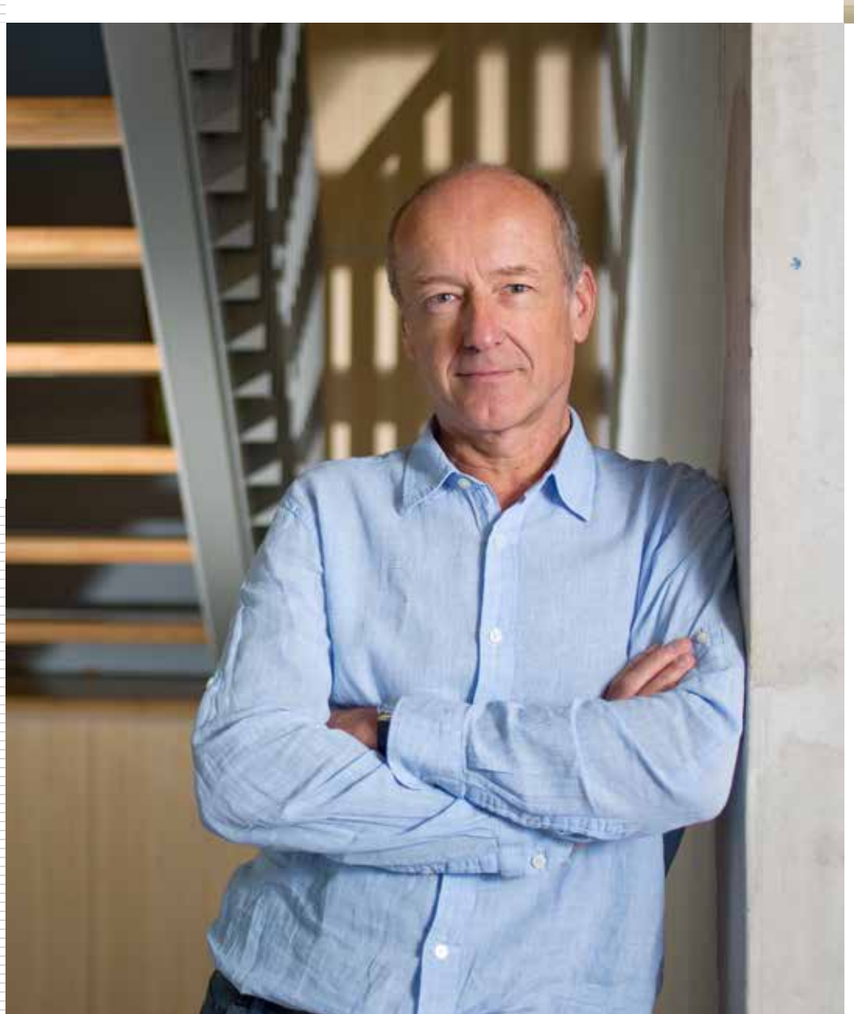
Biosketch

2011 – 2016
Founding Scientific Director, ERIBA, UMCG, Groningen, NL

2011 – present
Group Leader, Genetic Instability Ageing Center, ERIBA, UMCG, Groningen, NL

1998 – present
Group Leader, Genetic Instability Ageing Center, ERIBA, UMCG, Groningen, NL

1986 – present
Distinguished Scientist, BC Cancer Agency, Vancouver, CA



Research in our laboratory is aimed at understanding the role of genome instability in stem cells in relation to disease processes and ageing. The focus is on the role of specific helicases and guanine-rich DNA sequences in genome instability and stem cell function and, more generally, on the molecular mechanisms that regulate stem cell self-renewal and differentiation.

For these studies we have developed novel techniques including those to measure the telomere length in individual chromosomes and cells using fluorescence in situ hybridization, and single cell sequencing techniques with selectivity for DNA strands that are used as templates for DNA replication (Strand-seq).

We have established the ERIBA single cell sequencing platform, which is providing new insights into many biological processes. The platform also serves as a core facility for scientific collaborations. Highlights enabled by the Strand-seq technique are the identification of polymorphic inversions in human genomes, the assembly of whole chromosome haplotypes, and the fine mapping of sister chromatid exchange events in cells from patients with Bloom syndrome. An example of a Strand-seq result is shown in Figure 9.

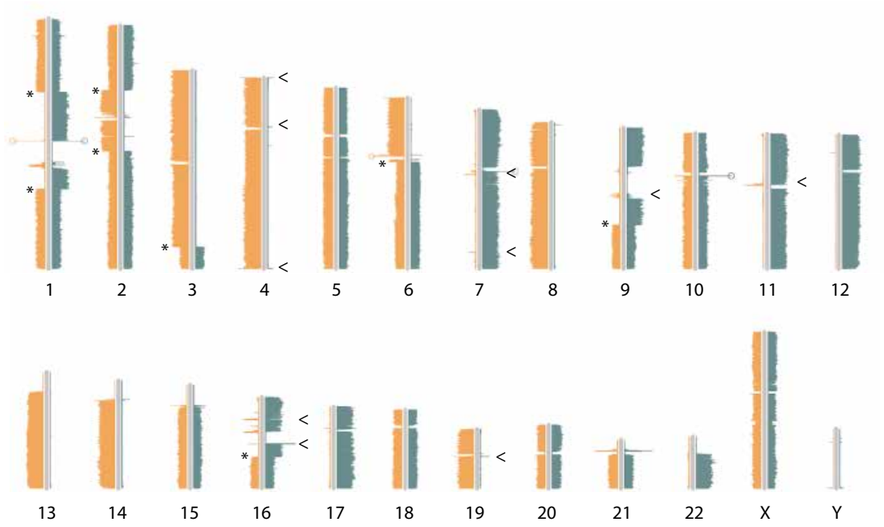


Figure 9. Strand-seq analysis of a human cell with a normal (diploid) set of chromosomes. Shown are sequencing reads mapping to defined intervals of either the "Watson" (orange) or "Crick" (blue/green) DNA template strand of the reference genome (numbers reflecting chromosome numbers). Note that sister chromatid exchange events (8 in total indicated by asterisks) and several polymorphic inversions (arrows) are observed. Reads mapping to either the Watson or the Crick strand (e.g. chromosome e.g. 5, 6, 10, 15 18, 20 and parts of several other chromosomes) can be used to assemble parental haplotypes without studies of the parental DNA.
The single cell sequencing approach is also used to measure the chromosomal content in different cell types. For example, we have studied the role of aneuploidy (abnormal chromosome number) in brain cells from patients with Alzheimer's disease and normal individuals. In contrast to what had been suggested in the literature, no increase in the number of aneuploid cells was observed in Alzheimer's disease. The role of aneuploidy in tumor cells was studied in collaboration with Floris Foijer and Maria Colomé-Tatché and others in and outside the UMCG.

Future Directions

The Strand-seq technique has widespread applications in studies of genome instability and ageing ranging from the identification of polymorphic inversions and parental haplotypes to the mapping of sister chromatid exchange events and structural variations in cells including numerical chromosomal abnormalities. Cells of interest include cells from patients with diseases resulting from heritable disorders of DNA repair and accelerated ageing as well as normal individuals participating in the LifeLines project in Groningen. Studies of stem cells, genome instability and ageing typically use cells from patients and animal models in collaboration with researchers and clinicians in and outside ERIBA.

The Lansdorp Group will continue to develop and use its single cell sequencing platform to address questions about genomes and genome instability in normal biology, ageing and diseases.To this end we will collaborate with colleagues within ERIBA and the UMCG as well as investigators throughout the world.

SELECTED PUBLICATIONS

Sanders, A.D., Hills, M., Porubsky, D., Guryev, V., Falconer, E. and **Lansdorp, P.M.** (2016) Characterizing polymorphic inversions in human genomes by single cell sequencing. Genome Res 26, 1575.

Porubsky, D., Sanders, A.D., Wietmarschen, N.v., Falconer, E., Hills, M., Spierings, D.C.J., Bevova, M.R., Guryev, V. and **Lansdorp, P.M.** (2016) Direct chromosome-length haplotyping by single cell sequencing. Genome Res 26, 1565.

van den Bos, H., Spierings, D.C., Taudt, A.S., Bakker, B., Porubsky, D., Falconer, E., Novoa, C., Halsema, N., Kazemier, H.G., Hoekstra-Wakker, K. et al. (2016) Single-cell whole genome sequencing reveals no evidence for common aneuploidy in normal and Alzheimer's disease neurons. Genome Biol, 17, 116.

Bakker, B., Taudt, A., Belderbos, M.E., Porubsky, D., Spierings, D.C., de Jong, T.V., Halsema, N., Kazemier, H.G., Hoekstra-Wakker, K., Bradley, A. et al. (2016) Single-cell sequencing reveals karyotype heterogeneity in murine and human malignancies. Genome Biol, 17, 115.

GROUP MEMBERS

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David Porubsky · Doctoral student
Hilda van den Bos · Doctoral student
Niek van Wietmarschen · Doctoral student
Nancy Halsema · Tecnician
Karin Hoekstra-Wakker · Technician
Jorn Staal · Technician

Ellen Nollen
Group Leader of the Laboratory Molecular Neurobiology of Ageing

Biosketch

2012 – present
Group Leader of the Laboratory of Molecular Neurobiology of Ageing, European Research Institute for the Biology of Ageing, University Medical Center Groningen, University of Groningen, NL

2012 – present
Professor (tenure track), University of Groningen

2006 – 2012
Assistant professor, Rosalind Franklin Fellow, Dept. of Genetics, UMCG, Groningen

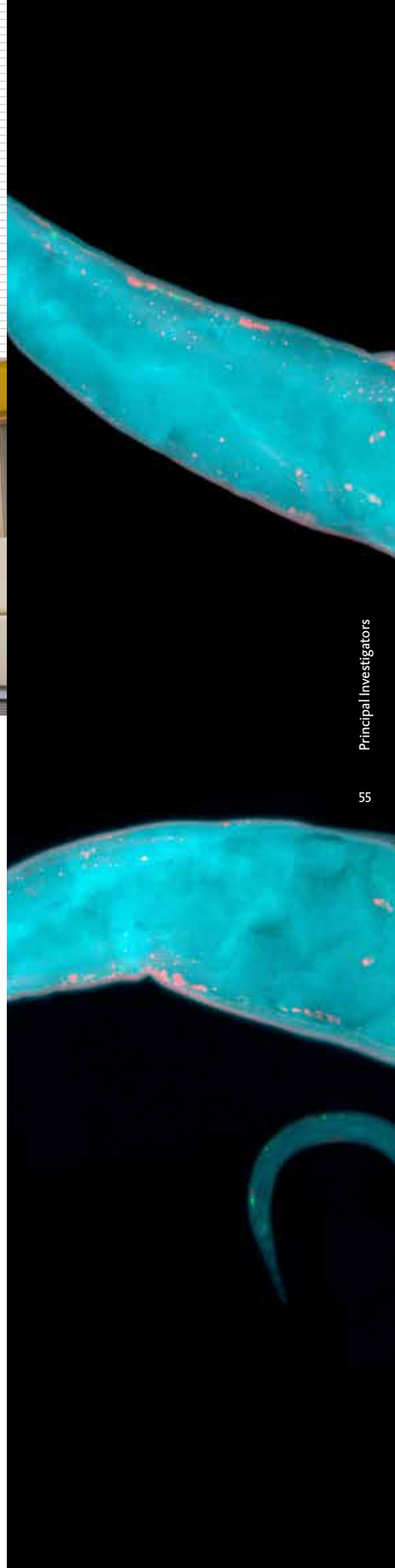
2002 – 2006
Postdoctoral fellow, Hubrecht Laboratory, Utrecht, Mentor: Dr. Ronald Plasterk

2000 – 2002
Postdoctoral fellow, Northwestern University, Evanston, USA, Mentor: Dr. Rick Morimoto

'By uncovering molecular mechanisms that drive age-related protein toxicity we hope to find drug targets for neurodegenerative diseases'

Our aim is to understand the molecular mechanisms that drive age-related toxicity of aggregation-prone proteins, which plays a role in age-related diseases like Parkinson and Alzheimer. Young and healthy cells have the capacity to refold, remove or sequester aggregation-prone proteins. During ageing this capacity is thought to decline and toxic aggregation-prone proteins accumulate, which in brain can lead to loss of neuronal function and cell death.

Using genetic screens in the nematode worm *C. elegans*, we have identified several of genetic modifiers of protein aggregation, which include MOAG-4/SERF and MOAG-2/LIR-3.These MOAGs can drive protein aggregation, independently of any co-factor, and their removal suppresses protein aggregation. We recently showed that in presence of aggregation-prone proteins, MOAG-2/LIR-3 acquires this aggregation-promoting function, switching from normally being a regulator of RNA-polymerase III transcription. For MOAG-4/SERF, we do not know its function in healthy cells. We have shown that its role in



aggregation is evolutionary conserved in human cells and that it acts on several amyloid-like proteins to promote their aggregation, which may become detrimental in age-related diseases.

Similarly, we identified tryptophan- 2,3 dioxygenase 2 (TDO-2) as a metabolic modifier of protein toxicity. Depletion of TDO-2 increases lifespan and protects against toxicity of different neurodegenerative disease proteins. Using transcriptome profiling in C. *elegans* we have identified cellular responses to tdo-2 depletion. We have worked out one of these responses and identified other amino-acid dioxygenases of which depletion results in the same health benefits previously observed for TDO-2 depletion in C. *elegans*. Because MOAG-4, TDO-2, and the other amino-acid dioxygenases are evolutionary highly conserved in human, their inhibition can be further explored as a strategy to suppress protein toxicity in disease (Figure 10).

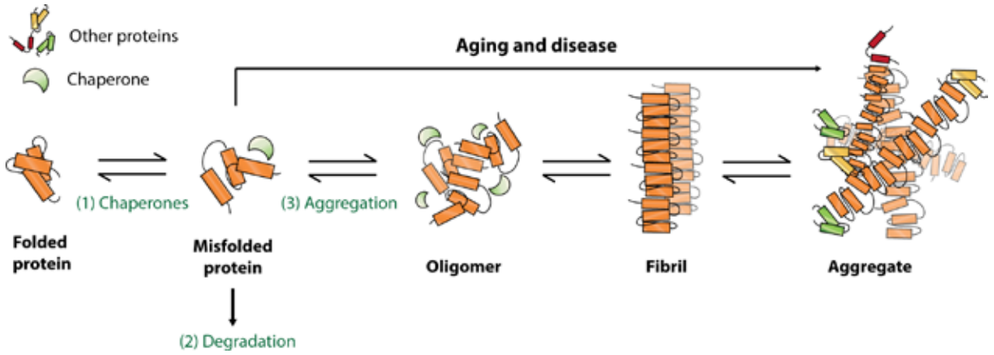


Figure 10. Protein aggregation during ageing and age-related diseases. Aggregation-prone proteins in cells are refolded (1) or degraded (2) and otherwise aggregate (3). During ageing, these aggregation-prone proteins accumulate, which is thought to cause cellular dysfunction and age-related diseases by unknown mechanisms. Uncovering the molecular mechanisms that drive the aggregation and toxicity of aggregation-prone proteins is the aim of our research (Koopman and Stroo, unpublished).

Future Directions

In the next five years our research will be focused understanding the mechanisms by which MOAGs and amino acid dioxygenases drive toxicity and aggregation of aggregation-prone disease proteins. Results from worms will be translated to (patient) cell models and mouse models for disease. Together with industrial partners, assays will be developed to search for compounds that inhibit these drivers to suppress protein aggregation and toxicity. These studies will provide fundamental insight into how organisms cope with toxic aggregation-prone proteins and yield candidate compounds to ameliorate protein toxicity in ageing and age-related diseases.

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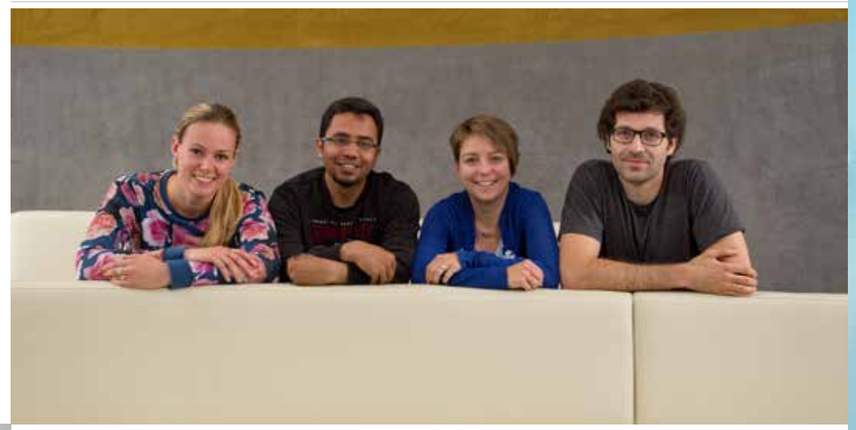
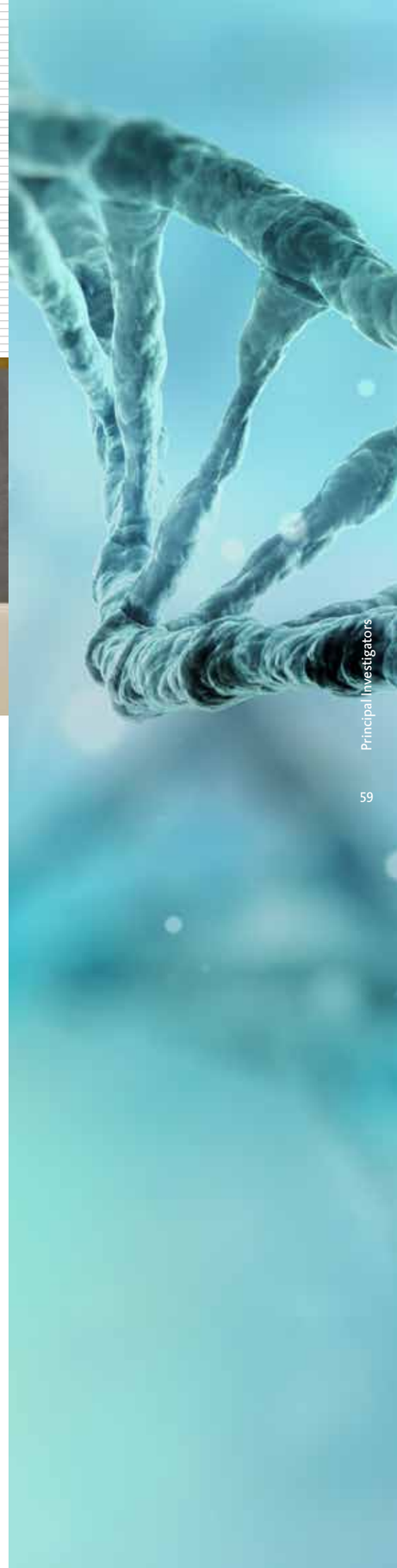
Anita Pras · Doctoral student
Esther Stroo · Doctoral student
Helen Michels · Doctoral student
Mandy Koopman · Doctoral student
Renée Seinstra · Technician
Wyste Hogewerf · Technician

Katrin Paeschke
Group Leader of the Laboratory of Nucleic Acids Structure and Repair

'G-quadruplex structures: a new mystery in genome stability'





Biosketch

2016 – present
Group Leader of the Laboratory of Nucleic Acids Structure and Repair, European Research Institute for the Biology of Ageing, University Medical Center Groningen, University of Groningen, NL

2012 – 2017
Group Leader of the Laboratory of Genome Stability, Dept. of Biochemistry, University of Würzburg, Würzburg, Germany

2007 – 2011
Research Scientist at the Department of Molecular Biology, Princeton University, NJ, USA
Post-doctoral fellow in the Laboratory of Prof. Dr. Virginia A. Zakian

2003 – 2006
Doctoral student at the Department of Cell Biology, University of Witten/ Herdecke, Germany

The particular focus of our group is to understand the nature and role of secondary structures that form within nucleic acids. In recent years, a special structure that can form within guanine rich sequences, in DNA and RNA, became of interest to many research fields. This structure is named G-quadruplex (G4). Due to their high stability they block biological processes such as DNA replication, transcription or telomerase function.

G4 structures are believed to be novel powerful regulatory components of the cell and fine-tune biological processes (Figure 11). However, these structures also challenge genome and RNA stability and proteins are needed that dissolve these structures in a timely manner to avoid misregulation of cellular processes.

We use a combination of genetic, molecular biological, and genome-wide approaches to identify and characterize novel G4-interacting proteins. Initial experiments were performed using yeast as a model organism and gained information will be transferred into human cells, to explore

their relevance for human health. We have developed three novel screening techniques that enable us to identify novel G4 interactions. Candidate proteins are validated in vitro as well as in vivo.

The regulation of G4 structures is tightly connected to helicase function. To this date multiple DNA helicases have been identified that unwind G4 structures and by this preserve genome stability (e.g. Bloom, Werner), but so far little is known about RNA helicases and G4 structures. We have identified and characterized two novel proteins that bind and/or unwind G4 structures. Screening results were confirmed by biochemical studies. Global analysis such as ChIPseq, PAR-CLIP, RNAseq and ribosome profiling further revealed information about protein binding and function. Global approaches were complemented by genetic assays. In summary, our group has developed a suit of genetic tools, which measure quantitatively genome stability upon the formation of G4 structures.

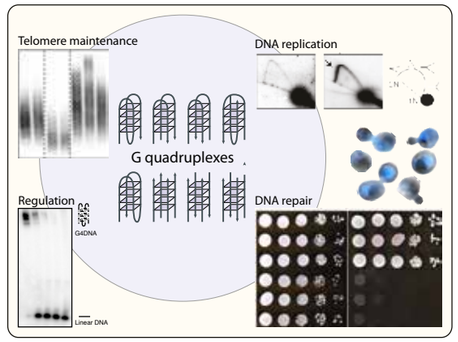


Figure 11. G-quadruplex structures are highly diverse, secondary DNA or RNA structures (cartoon in the center of the image), which can form in vivo under specific conditions. In recent years it has been shown that they influence biological processes, such as DNA replication, DNA repair, telomere maintenance, transcription, or translation (examples of experiments addressing these G4 dependent changes of processes are depicted). Specific proteins are required to regulate the formation and unwinding of these structures in order to support genome stability. This figure depicts also results of different experimental approaches performed in our laboratory.

Future Directions

The overall goal of the research in our group is to elucidate the impact of G4 structures on biological processes. We will identify and characterize novel G4 interactors that are essential for G4 maintenance, function, and repair. Our future experiments will provide information on when and which G4 structures form and which impact they have on genome stability and ageing. Due to the connection of G4 structures to cancer and other genetic diseases this data will be of great interest for medical research. Studies with G4 specific ligands that stabilize or induce G4 will be of great relevance for medical scientists who aim to use these ligands as an anti-proliferation drug in cancer treatments. Our work, aimed to understand G4 structure regulation and function and the proteins involved, is essential to develop G4 specific drugs in order to evaluate the risks and rewards of such an approach.

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Philips JA, Chan A., **Paeschke K#**, Zakian VA#. (2015), The Pif1 helicase, a negative regulator of telomerase, acts preferentially at long telomeres. PLoS Genet. Apr 23, 11 (4) (#shared corresponding author)

Paeschke K*, Bochman ML*, Zakian VA. (2014), Hrq1, a homolog of the human RecQ4 helicase, acts catalytically and structurally to promote genome integrity. Cell Rep. Jan 30,6(2):346-56.

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Paeschke, K., Capra, J.A., Zakian V.A. (2011) DNA replication through G-quadruplex motifs is promoted by the *S. cerevisiae* Pif1 DNA helicase. Cell May 27th ;145(5):678-91.

(*co-first authors).

GROUP MEMBERS

LABORATORY GRONINGEN
Satya Pandey · Postdoctoral fellow
Eike Schwindt · Doctoral student
Enikö Fekete-Szücs · Doctoral student
Claudia Gasso · Master Student
Inge Kazemier · Technician

LABORATORY WÜRZBURG
Silvia Götz · Doctoral student
Markus Sauer · Doctoral student
Yang Qianlu · Guest Scientist
Maria Gessler · Technician

Judith Paridaen
Group Leader of the Laboratory of Asymmetric Cell Division and Ageing

‘Understanding how microscopic processes within single stem cells affect their function is essential to answer how stem cells shape and can help to maintain a healthy body.’

Biosketch

2016 – present
Junior PI/Rosalind Franklin Fellow at ERIBA

2009 – 2015
Postdoctoral fellow, Max Planck Institute for Molecular Cell Biology and Genetics, Dresden, Germany. Advisor: Prof. Dr. W. Huttner

2004 – 2009
Doctoral research, Hubrecht Institute for Developmental Biology and Stem cell research, and Utrecht University; Formal promotor: Prof. Dr. H. Clevers, Daily advisor: Dr. D. Zivkovic

2003
M.Sc. Biomedical Sciences, Utrecht University

Stem cells act in developing and adult organisms to produce all specialized mature cells in the body. When stem cells divide, they select a particular division mode that is symmetric or asymmetric. The symmetry of this division mode determines how many specialized and stem cell daughter cells are generated per division. Defective division mode selection is implicated in developmental disorders, diseases such as cancer, and ageing.

Although some of the contributing mechanisms have been identified, it is still unclear how and when stem cells select division mode and daughter cell fates. We aim to identify molecular mechanisms that regulate stem cell function at the single-cell level. In particular, we study the role of heritable subcellular structures, signaling pathways and dynamics of gene expression in symmetric and asymmetric stem cell divisions. The main model organisms are the zebrafish and mouse. Ultimately, the aim is to understand how the accumulated sum of all stem cell divisions leads to generation and maintenance of healthy adult tissues, and how stem cells can be controlled to regenerate lost or damaged tissues.

One of the cellular structures that we study is the centriole. Centrioles within the cell are inherently asymmetric due to different age and composition. After cell division, centrioles are distributed between daughter cells. We showed that the older centriole is inherited, together with a remnant from a key signaling organelle, the primary cilium, into daughter cells that remain stem cells (Figure 12). These daughter cells reform a functional cilium earlier than differentiating daughter cells. The hypothesis is that this mechanism contributes to daughter cell asymmetry in asymmetric stem cell divisions.

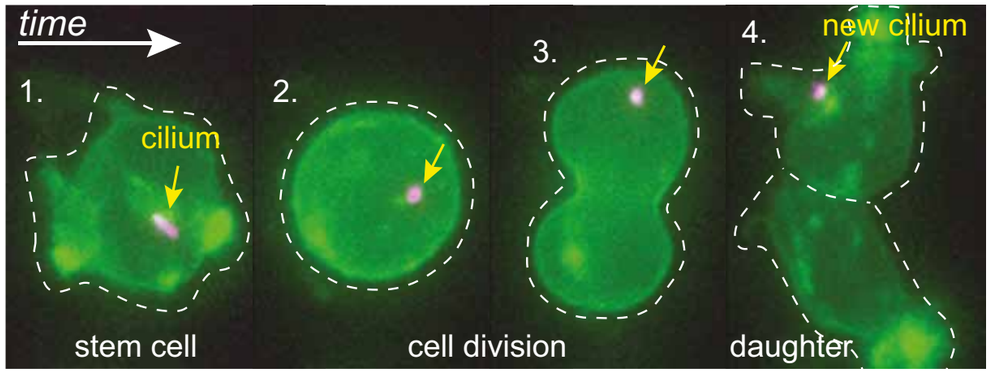

Figure 12. Inheritance of mother centriole and ciliary remnant in dividing embryonic neural stem cells. The plasma membrane (green), centrioles (green) and ciliary membrane (magenta) of the neural stem were labelled to allow time-lapse imaging (Paridaen et al., 2013).

Future Directions

Our aim is to further our understanding of individual stem cell function by studying the behavior of neural stem cells in the developing and adult brain. To this end, we are developing new signaling reporter assays to study the link between signaling activity dynamics and cell fate selection. Stem cell heterogeneity will be analyzed using single-cell genomic analyses and time-lapse live imaging of developing embryos. Lastly, computational modeling will be used to describe and predict (new) aspects of decision-making and heterogeneity therein by stem cells in the developing brain. In the future, these analyses will be extended into adult and ageing brains. The goal is to develop computational models that accurately predict the effect of manipulating stem cells in vitro and in vivo, which could aid in treatment and prevention of disease and ageing.

SELECTED PUBLICATIONS

Paridaen JTML, Huttner WB, Wilsch-Bräuninger M (2015). Analysis of primary cilia in the developing mouse brain. Methods Cell Biol. 127, 93-129.

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Paridaen JTML, Wilsch-Bräuninger M, Huttner WB (2013). Asymmetric inheritance of centrosome-associated primary cilium membrane directs ciliogenesis after cell division. Cell. 155:333-44.

GROUP MEMBERS

Glòria Casas Gimeno · Doctoral Student

Liesbeth Veenhoff
Group Leader of the Laboratory of Cellular Biochemistry

‘Studying biology in time is an unbiased way to reveal fundamental knowledge, knowledge which is needed to combat age-related diseases.’

Biosketch

2015 – present
Associate Prof. tenure track, European Research Institute for the Biology of Ageing, University Medical Center Groningen, University of Groningen, NL

2010 – 2015
Assistant Prof. tenure track, in ERIBA as of 2012, University Medical Center Groningen, University of Groningen, NL

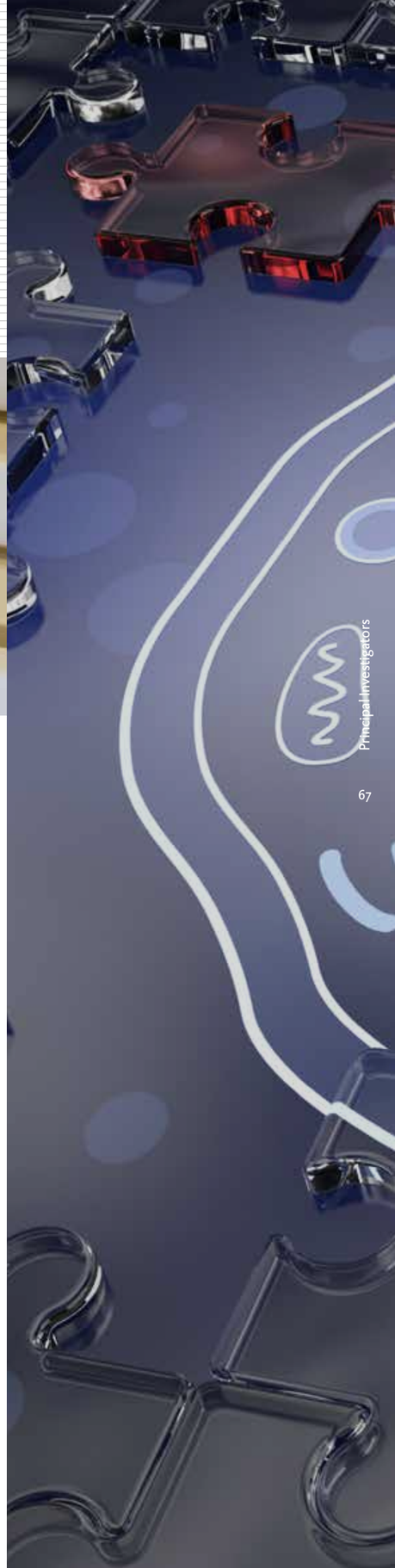
2004 – 2010
Post-doctoral Veni & Vidi fellow, University of Groningen, NL

2002 – 2003
Post-doctoral HFSP fellow with Prof. Michael P. Rout, Rockefeller University, New York, USA

1996 – 2001
Doctoral student. student with Prof. Bert Poolman, cum laude, University of Groningen, NL

Our laboratory is fascinated by the workings of molecular machines. The nuclear pore complex is one of the largest molecular machines in a cell. It is embedded in the nuclear envelope, where one of its prime tasks is to mediate selective transport to and from the nucleus. Through this selective transport, of e.g. transcriptional regulators and mRNAs, it has a critical role in defining a cells identity and physiology.

At present we have a good level of understanding of what a nuclear pore complex looks like in young cells, and how it performs its transport function. Outstanding questions that our laboratory contributed to are related to the structure of the selectivity barrier of the nuclear pore complex and the mechanism of transport of membrane proteins. In aged cells, we know very little about how and if the functioning of the nuclear pore complex is safeguarded and how this impacts cell physiology. We aim to contribute to our understanding of how the nuclear pore complex is mplicated in ageing.



Our laboratory addresses their questions in the single cell eukaryote *Saccharomyces cerevisiae*, or baker's yeast, in which system-wide and single-cell studies can be performed under well controlled genetic and environmental conditions. This is important because this tackles two of the main challenges in ageing research, namely that ageing is multifactorial and that it is highly individual.

In a large collaborative project, we generated the first systems-level view of the changes in the proteome and transcriptome of replicative ageing yeast (Figure 13). We found that major signatures of ageing cells are (i) a decreasing correlation between the transcriptome and the proteome and (ii) altered stoichiometry in protein complexes. This loss of stoichiometry was particularly strong for the nuclear pore complex suggesting declining quality control and function of nuclear pore complexes in ageing.

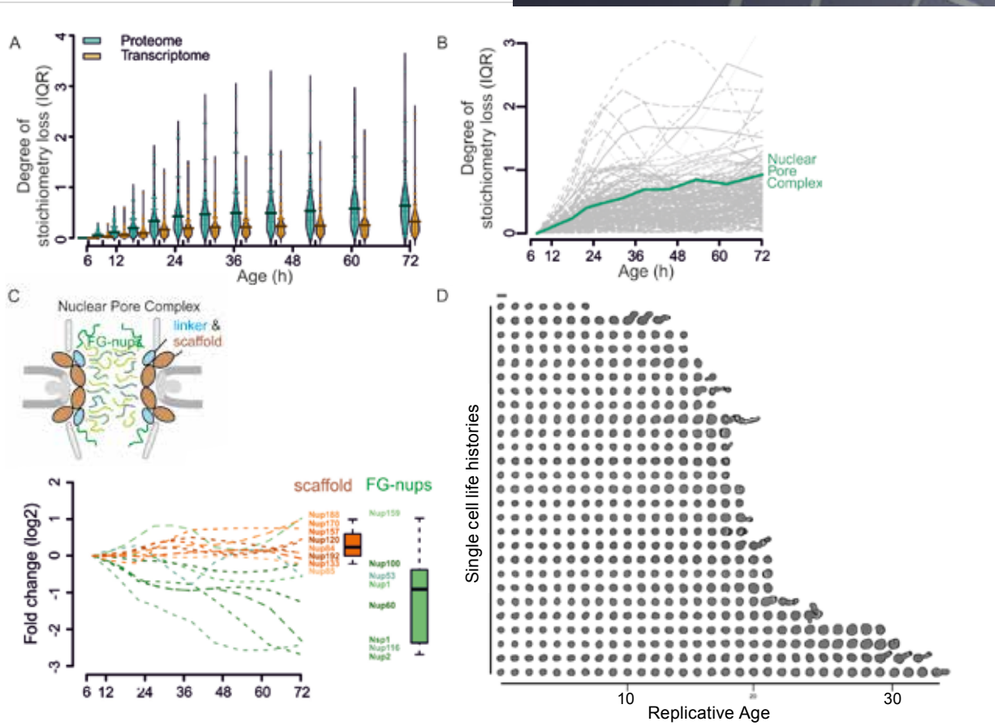


Figure 13. Stoichiometry loss during ageing (for a single complex defined as the Interquartile (IQR) of distribution of fold change of components) increases with ageing, mostly so on the proteome level. (B) Loss of protein stoichiometry in all complexes during ageing (grey lines), with the NPC highlighted in green. (C) Cartoon of NPC structure . The protein abundance changes (log2 scale) of the NPC components are plotted in time showing the scaffold components are relatively stable in ageing while unfolded FG-nups are changing to different degrees. D. Example of individual life span histories obtained in microfluidic chips highlighting that cells have variable replicative lifespans even in the absence of genetic or environmental variation. Cells were imaged after each division.

Future Directions

There is emerging evidence that changes in nuclear pore complex function go hand in hand with loss of protein homeostasis during ageing and in several neurodegenerative diseases. In the coming years we intend to provide a system wide view of the dynamics of turnover and inheritance in ageing yeast cells identifying ageing markers, and to provide insight into heterogeneity of replicative ageing process. These system wide characterizations of the ageing process will be complemented with dedicated studies to unravel nuclear pore complex structure and function in ageing.

SELECTED PUBLICATIONS

Janssens GE, Meinema AC, González J, Wolters JC, Schmidt A, Guryev V, Bischoff R, Wit EC, **Veenhoff, LM***, Heinemann, M*, Protein biogenesis machinery is a driver of replicative ageing in yeast eLife. 2015 Sep 30;4. doi: 10.7554/eLife.08527 *Shared last author

S Kralt A, Noorjahan B.J, van den Boom V, Lokareddy RK, Steen A, Cingolani G, Fornerod M, and **Veenhoff LM**, Conservation of inner nuclear membrane targeting sequences in mammalian Pom121 and yeast Heh2 membrane proteins. Mol Biol Cell. 2015 26(18):3301-12

S Lokareddy RK, Hapsari RA, van Rheenen M, Pumroy RA, Bhardwaj A, Steen A, **Veenhoff, LM*** and Cingolani G*, Distinctive properties of the Nuclear Localization Signal of Inner Nuclear Membrane proteins Heh1 and Heh2, Structure. 2015;23(7):1305-16. *Shared last author

S Popken P, Ghavami A, Onck PR, Poolman B, **Veenhoff LM**. Size-dependent leak of soluble and membrane proteins through the yeast nuclear pore complex. Mol Biol Cell. 2015;26(7):1386-94.

GROUP MEMBERS

Jannie de Jong · Technician
Anton Steen · Postdoctoral fellow
Irina Schmidt · Doctoral student
Marije Semmelink · Doctoral student

3. Research Collaborations

Collaborations within the University Medical Center Groningen and the University of Groningen

Scientists at ERIBA collaborate locally with many Departments in the UMCG and the University of Groningen. In the following pages we present an overview of the major collaborations. Some of these collaborations (flagged in blue) have been initiated by specific start-up funds from the ERIBA budget. These 50k ERIBA Research Grants were intended to serve as seed funds to kick-start joint experiments between ERIBA and UMCG/RUG labs, for which subsequently larger scale grants were to be obtained. Other collaborations have been supported through alternative funding schemes.

		Roles of microRNAS in heart failure
ERIBA	**Dept. of Cardiology**	The goal of the project is to establish the role of microRNAs in the pathophysiology of heart failure.
E. Berezikov E. Ovchinnikova	A. Voors R. de Boer P. van der Meer	This project was initiated in 2012. It has resulted in 3 publications and 1 patent application. Eur J Heart Fail. 184:414-23 (2016); Int J Cardiol. 203:564-9 (2016); Int J Cardiol. 224:231-239 (2016).

		Exploring C/EBPβ-LIP as a biomarker and target in breast cancer
ERIBA	**Dept. Medical Oncology**	The goal of the project is to develop a biomarker against the oncogene C/EBPβ-LIP.
C. Calkhoven	M. Jalving	Intended starting date: 01.01.17.

		System wide view of yeast replicative ageing
ERIBA	**Depts. of Systems Biology, Probablity and Statistics, Analytical Biochemistry**	The goal of the project was to generate a system wide view of proteome and transcriptome changes in ageing yeast cells in order to answer what may be early causes of cellular ageing.
L.M. Veenhoff V. Guryev G.E. Janssens	M. Heinemann E.C. Wit R. Bischoff	This project was initiated in June 2011. It has resulted in 1 publication (Elife. 2015 Dec 1;4:e08527), and 290 Euro additional funding.

		Microfluidic devices for yeast ageing research
ERIBA	**Pharmaceutical Analysis (Groningen Research Institute of Pharmacy/GRID)**	The project aims at developing new microfluidic chips for ageing research.
L.M. Veenhoff I.L. Schmidt	E.M.J. Verpoorte	This project was initiated in September, 2014.

		Nuclear Pore Complex structure and function
ERIBA	**Zernike Institute for Advanced Materials Department of Biochemistry**	The project aimed at understanding how the disordered phase of the nuclear pore complex presents a selective barrier.
L.M. Veenhoff A. Steen	Onck, P.R. B. Poolman	This project was initiated in September, 2013. It has resulted in 2 publications (Mol Biol Cell. 2015 Apr 1;26(7):1386-94, Biophys J. 2014 Sep 16;107(6):1393-402), 1 joint grant proposal, and 260 Euro additional funding.

		Consequences of chromosomal instability for skin ageing and carcinogenesis
ERIBA	**Dept. of Dermatology**	The project aims at investigating the role of aneuploidy in skin carcinogenesis and skin ageing.
F. Foijer J.M. Garcia P.M. Lansdorp	M. Jonkman M. Pasmooij J.Terra	This project was initiated in March 2014. It has resulted in 1 review so far, and one research paper in preparation. We plan to apply for additional funding when our research paper will be published.

		Time-lapse imaging of DNA damage and cell fate
ERIBA	**Dept. of Medical Oncology**	This project aims at better understanding the cellular fates in response to DNA damage.
Floris Foijer	Marcel van Vugt	Several projects were done in close collaboration between both labs. So far they yielded one publication (Proc Natl Acad Sci U S A. 2015 Dec 8;112(49):15160-5) and another manuscript submitted.

		Identifying the role of Prmt5 in aneuploid cancer
ERIBA	**Dept. of Pediatrics**	In this project, we decipher the biology of Prmt5 as a frequently upregulated gene in aneuploid cancer.
Floris Foijer	Kathrin Thedieck	This collaboration has yielded two studies that are currently being prepared for publication.

		Chromosomal instability in pediatric cancers
ERIBA		In this collaboration with the department of pediatric oncology, we study aneuploidy in pediatric B-ALL and medulloblastoma.
Floris Foijer, Peter Lansdorp, Victor Guryev	Eveline de Bont, Sophia Bruggeman	This project was initiated in 2012 and is funded by SKOG (Groningen Foundation for Pediatric Oncology; 2.5 million Euro). We plan to apply for follow up funding when the SKOG funding runs out.

		Clonal behavior of pediatric leukemia
ERIBA	**Pediatric Oncology/ Pediatrics**	The project aims to establish the clonal heterogeneity of primary pediatric leukemias.
G. de Haan	E. de Bont E. Verhagen M.Belderbos	This project was initiated in June 2013. It has resulted in 2 published publications (Genome Biol. 2016 May 31;17(1):115, Methods Mol Biol. 2016;1516:57-89) and 1 submitted paper. It has resulted in two awarded grant applications from the Dutch Cancer Society (totalling 550k).

		Salivary gland biology
ERIBA	**Dept. of Cell Biology**	This is a long-term collaboration aimed to identify and functionally characterize salivary gland stem cells for autologous transplant procedures.
G. de Haan	R.C. Coppes	This project was initiated in 2006. It has resulted in 7 joint publications, 4 of which between 2014-2016 (Stem Cell Reports. 2014 Dec 9;3(6):957-64, Radiother Oncol. 2015 Sep;116(3):443-8, Stem Cell Reports. 2016 Jan 12;6(1):150-62, Stem Cells. 2016 Mar;34(3):640-52). It has resulted in several awarded grant applications from the Netherlands Institute for Regenerative Medicine and NWO/ZonMW.

		Chemotherapy-induced senescence
ERIBA	**Dept. of Oncology**	The goal of the project is to identify and characterize senescent cells in patients with testicular cancer treated with chemotherapy.
M. Demaria J. Kohli	J. Gietema S. Lubberts C. Mayer	This project was initiated in November 2015. It has resulted in preliminary data which will be used to apply for a joint Dutch Cancer Society grant.

		Generation of anti-senescence and melanoma antibodies
ERIBA	**Groningen Research Institute of Pharmacy/GRID**	The project aims at identifying antibodies that re-activate immune response against senescent melanocytes and melanoma cells.
M. Demaria A. Soto-Gamez	Y. Boersma	This project was initiated in April 2016. It has resulted in a 4-year doctoral scholarship for Abel Soto-Gamez.

		Cellular senescence in cardiac disease
ERIBA	**Dept. of Cardiology**	The project aims at characterizing the role of senescent cells in different models of cardiac dysfunctions.
M. Demaria A. Hernandez-Segura	P. Meer van der H. Sillje	This project was initiated in December 2015. Currently preparing application for the Dutch Heart Foundation.

		Nanodiamonds and yeast
ERIBA	**Dept. of Biomedical Engineering**	This project aims to use nanodiamonds to study yeast ageing.
D. Novarina M. Chang	S.R. Hinterding M.V. Koot E. Ellermann S.R. Hemelaar F.P. Perona-Martinez D. Roig S. Hommelet H. Takahashi R. Schirhagl	This project was initiated in 2014. It has resulted in one submitted paper.

		Amino-acid metabolism in ageing and age-related diseases
ERIBA	**Dept. of Laboratory Medicine**	Aim is to establish the role of amino-acid degrading enzymes in ageing and age-related proteotoxicity.
E. Nollen	Ido Kema Martijn van Faassen	This project has been funded by the ERC stg, has resulted in 1 publication (Proc Natl Acad Sci U S A. 2012 Sep 11;109(37):14912-7), two manuscripts, 1 ongoing MD Doctoral fellowship, and 1 patent application.

		Amino-acid metabolism in ageing and age-related diseases
ERIBA	**Dept. of Neurology**	Aim is to establish the role of amino-acid degrading enzymes in ageing and age-related proteotoxicity.
E. Nollen	P.P. de Deyn F. Sorgdrager	This project is funded by an MD Doctoral fellowship.

		Coenzyme A metabolism
ERIBA	**Dept. of Cell Biology**	Aim is to understand the molecular regulation of Coenzyme A metabolism using *C. elegans.*
E. Nollen	O. Sibon M. Baratashvili	This project has resulted in 2 publications (EMBO Mol Med. 2011 Dec;3(12):755-66, Nat Chem Biol. 2015 Oct;11(10):784-92).

		MYC-microRNA regulation in B cell lymphoma
ERIBA	**Dept. of Pathology**	The project examines the control of mTORC1-signaling by MYC through the regulation of microRNAs in the context of B cell lymphoma.
C.F. Calkhoven	J.H.M. van den Berg J. Kluiver	The project was initiated in 2011. It resulted in a manuscript now in revision. The project was funded by the Deutsche Krebshilfe (250k), ERIBA and UMCG.

		Oncogenic functions of C/EBPβ-LIP in triple negative breast cancer
ERIBA	**Dept. of Medical Oncology, MCCA, Dutch Cancer Institute (NKI) Amsterdam, Max Delbrück Center (MDC) Berlin**	The project aims to understand the role of C/EBPβ-LIP in cancer metabolism and metastasis in the context of breast cancer.
C.F. Calkhoven	J. Jonkers, NKI, Peter Bouwman, NKI, I. Huijbers, MCCA-NKI, S. Kempa, MDC, Berlin, C. Schröder and H. Jalving, UMCG.	The project was initiated in 2016. Resulted in a KWF grant (€M 670).

		Exploiting the C/EBPβ-centered regulatory network that controls nutrition-mediated health effects
ERIBA	**Johann Bernoulli Institute**	We aim to exploit the metabolic transcription factor C/EBPβ-centered gene-regulatory network to reduce the complex nutrition–health relationships to the single readout of C/EBPβ-LIP expression.
C.F. Calkhoven V. Guryev	M. A. Grzegorczyk	The project was initiated in 2016. An application for an NWO grant is filed.

		Multi-omics characterization of lymphoblastic leukemia
ERIBA	**Pediatric Oncology / Pediatrics**	Project aims for better understanding of lymphoblastic leukemia through integration of genome, transcriptome and kinome profiles of cancer samples.
V. Guryev	E. de Bont	Project started in 2012 and has resulted in 5 publications: Leukemia. 2014. 28:589-99; Proteomics. 2015. 15:1245-54; Oncotarget. 2015. 6:14970-81. Exp Hematol Oncol. 2015. 4:23; Genome Biol. 2016.17:115.

		Proteogenomics approach to chronic obstructive pulmonary disease (COPD)
ERIBA	**Pathology, Pulmonary diseases, Pharmacy, RUG**	The aim of the project is to characterize transcriptome and proteome changes in COPD patients. Using Bayesean modeling we expect to discover key elements responsible for the disease and targets for its treatment.
V. Guryev	D. Postma W. Timens R. Bischoff M. Grzegorczyk	Project started in 2012 and has resulted in 2 publications: J Proteomics. 2016. 134:25-36. Adv Exp Med Biol. 2016. 926:21-47. We obtained funding for 1 Doctoral student position (Eu 200k through DSSC program).

		Whole genome sequencing analysis of Dutch individuals
ERIBA	**Dept. of Genetics**	Project aims at better mapping of structural variants in whole-genome and exome sequencing data.
V. Guryev	C. Wijmenga M.A. Swertz S. Zhernakova	Project started in 2011 and has resulted in 5 publications: Eur J Hum Genet. 2014. 22:221-7; Genome Res. 2015. 25:792-801; Nat Genet. 2015. 47:822-6. Eur J Hum Genet. 2016. 24:263-70; Nat. Commun. 2016. 7:12989.

		Effect of the RNA helicase RHAU on lung cancer development
ERIBA	**Dept. of Pulmonology**	
K. Paeschke	H. Groen	Project started in 2016, is part of grant application.

		Evaluating genomic heterogeneity at the single cell level as a predictor of response to treatment of lung cancer patients
ERIBA	**Depts. of Pulmonary Diseases and Pathology**	This project aims to provide insight into the potential tumor response prediction value of single cell whole genome sequencing in early- and advanced-stage lung cancer patients. By exploring the feasibility of Strand-seq we can further improve the potential predictive value of genomic ITH. Setting up the analysis of CTCs, may result in a much less invasive approach of obtaining tumor cells and will allow testing the predictive value of genomic heterogeneity of circulating tumor cells.
P. Lansdorp D. Spierings H.v.d.Bos	H. Groen J. Henneman A.v.d.Berg	This project was initiated in 2015. It has resulted in 1 published paper (Genome Biol. 2016 May 31;17(1):115) and 1 submitted paper. It also has resulted in a grant application to the Dutch Cancer Society.

		Genome instability in cultured salivary gland stem cells
ERIBA	**Dept. of Radiobiology**	The goal of this project is to test if stem cells cultured for possible in vivo transplantation are genetically normal.
P. Lansdorp D. Spierings	R. Coppes M. Maimets	We showed in this pilot project, initiated in 2014, that late passage cultured salivary gland cells show remarkable increases in a number of genomic regions containing specific genes including Lgr5, Tcf3, Dkk2 and EGF (in preparation for publication).

		DNA damage in hamster lymphocytes recovering from hibernation
ERIBA	**Dept. Clinical Pharmacology**	This project aims to provide insight into the DNA repair pathways operating in lymphocytes from hamster immediately following recovery from hibernation.
P. Lansdorp D. Spierings	R. Henning M. Tolouee Nodolaghi	Ongoing

Analysis of genomic instability and treatment effect in individual cancer cells

ERIBA	**Dept. Med. Oncology**	We aim to visualize the genomic landscape at a single-cell level to understand genomic instability in HR-deficient cancer cells, and to ultimately improve therapeutic targeting of these tumor cells.
P. Lansdorp D. Spierings A.M. Heyink	M.v.Vugt	This project was initiated in 2015 with help from the ERIBA start-up funds. It is ongoing and has already resulted in a grant application to the Dutch Cancer Society.

Chromosome copy number variations in ageing and cancer

ERIBA	**Depts. Path. and Neurological Sciences**	We aim to visualize chromosome copy number variations at a single-cell level in order to better understand ageing and tumor evolution.
P. Lansdorp, F.Foijer M. Colomé-Tatché D. Spierings, B.Bakker A. Taudt, V.Guryev	A.v.d.Berg W.Timens E. Boddeke W. den Dunnen	Projects were initiated in 2014. It has resulted in a publication (Genome Biol. 2016 May 31;17(1):115). Other papers are in preparation.

Distribution of newly formed histones over sister chromatids

ERIBA	**Dept. of Pharmacy**	The goal of this project is to study the distribution of newly formed histones and nucleosomes over the two sister chromatids in cells which can be recognized by sequencing of DNA template strands. The goal is to test the hypothesis that this novel histones are randomly distributed over sister chromatids as is typically assumed.
P. Lansdorp D. Spierings	F.Dekker M. Zwinderman	Ongoing

Telomere length measurements in the LifeLinesDeep cohort

ERIBA	**Dept. of Genetics**	The goal of this project is to study the telomere length in > 1000 normal persons participating in the LifeLines Deep project. The data wil be used to look for correlations with any of the many other measurements and biometric and psycho-social data available for this group.
P. Lansdorp S. Henkelman	S.Zhernakova	Analysis ongoing, paper expected 2017.

Role of structural variations in microdeletion syndromes

ERIBA	**Dept of Genetics**	The goal of this project is to study structural rearrangements in parental genomes that can be detected using Strand-seq as a cause of unexplained microdeletions or duplications in affected children.
P. Lansdorp D. Spierings	T. Dijkhuizen B.Raddatz C.v.Raavenswaaij	Ongoing

Chromatin structure in aneuploid tumors

ERIBA	**Depts. of Pediatrics/ Pediatric Oncology**	The projects aims at studying the chromatin structure of aneuploid cells from tumors.
M. Colomé-Tatché	S. Bruggeman	This project is a joint collaboration of the group of Maria Colomé-Tatché and F. Foijer at ERIBA and S. Bruggeman at the UMCG. It is being initiated now (currently hiring a postdoctoral fellow).

Overview of the most relevant national and international collaborations

Scientists at ERIBA collaborate with many researchers outside the Groningen area, in the Netherlands, Europe, and beyond. Here we document a selection of the most relevant of those collaborations, what they entail, how there are funded, and what the result of the partnership has been.

		Structural biology related to nuclear transport of membrane proteins
ERIBA		Mol Biol Cell. 2015 Sep 15;26(18):3301-12. Structure. 2015 Jul 7;23(7):1305-16.
L.M. Veenhoff	G. Cingolani, Thomas Jefferson University M. Fornerod, Erasmus MC, Rotterdam	Funded by the Netherlands Organization for Scientific Research (NWO/vidi to LMV).

		Single cell observations of nuclear transport in ageing
ERIBA		PLOS ONE, 2016, Nov. accepted.
L.M. Veenhoff	M. Crane, University of Washington	Funded by the Netherlands Organization for Scientific Research (SBC-EMA to LMV).

		Identification of microRNA125 targets
ERIBA		Cell Stem Cell. 2016 Sep 1;19(3):383-96.
G. de Haan	J. Dick, University of Toronto/S. Erkeland, Erasmus MC Rotterdam	Funded by Netherlands Institute for Regenerative Medicine and Netherlands Organization for Scientific Research (NWO/ZonMW).

		Identification of Cbx binding partners
ERIBA		Joint paper in preparation.
G. de Haan	R. Poot, Erasmus MC, Rotterdam/F.Hof Univ Victoria, Canada	Joint research grant awarded by Dutch Cancer Society.

		Marriage
ERIBA		Joint paper submitted with de Wind laboratory, joint paper with H.Geiger (Nat Rev Immunol. 2013 May;13(5):376-89).
G. de Haan	Multiple EU Scientists, including Niels de Wind, LUMC Leiden	FP7 EU funded Initial Training Network (http://www.ageingnetwork.eu).

		Defining the difference between a double-strand break and a telomere
ERIBA		Paper submitted and under review at eLife.
M. Chang	D. Durocher, Lunenfeld-Tanenbaum Research Institute/ University of Toronto	Funded by Netherlands Organization for Scientific Research (NWO/ALW).

		Centrosome amplification is sufficient to promote spontaneous tumorigenesis in mammals
ERIBA		Paper under revision (Developmental Cell).
F. Foijer P.M. Lansdorp	Andrew Holland, John Hopkins, Baltimore	Funded by NIH funds awarded to Andrew Holland.

		Tolerance to whole chromosome versus partial aneuploidies is determined by their differential effect on genomic stability
ERIBA		Paper submitted (Developmental Cell).
F. Foijer P.M. Lansdorp	René Medema, Netherlands Cancer Institute, Amsterdam	Funded by Dutch Cancer Society grants to Rene Medema and Floris Foijer.

		Mechanism of mitotic decline during natural ageing
ERIBA		Paper submitted (Science).
F. Foijer	Elsa Logarinho, I3S, Instituto de Investigação e Inovação em Saúde, Porto	Funded by FCT/MCTES (Fundação para a Ciência e a Tecnologia/Ministério da Ciências).

		PloidyNet: understanding the role of chromosomal instability in cancer
ERIBA		Various papers in preparation and first studies published.
F. Foijer	PloidyNet; coordinated by Netherlands Cancer Institute (René Medema) and ERIBA (Floris Foijer) 9 academic and 2 industrial laboratories throughout Europe.	Funded by EU FP 7Marie Curie Innovative Training Network Grant. (http://www.aneuploidy.nl).

ERIBA		Manuscript in preparation
E. Nollen	V. Reinke, Yale, USA	Identification of MOAG-2/LIR-3; ChIP-seq analyses of LIR-3 DNA binding sites. Funded by ERC and Ubbo Emmius Fonds.

ERIBA		Proc Natl Acad Sci U S A. 2012 Sep 11;109(37):14912-7.
E. Nollen	P. Oefner, University of Regensburg, Geramny	Role of tryptophan metabolism in protein toxicity; analyses of tryptophan metabolites and proteomics on tryptophan modifications in *C. elegans*. Funded by ERC.

ERIBA		Manuscript in preparation
E. Nollen	F. Mulder, University of Aarhus, Denmark	Structural changes of MOAG-4/SERF in amyloid aggregation. Doctoral student exchange.

ERIBA		Manuscript in preparation.
E. Nollen	E. Wanker, MDC Berlin, Germany	Protein interactions with SERF. Postdoctoral fellow and doctoral student exchange, funded by ERC.

ERIBA		Sci Adv. 2016 Feb 12;2(2):e1501244, Chemphyschem. 2011 Feb 25;12(3):673-80, J Mol Biol. 2010 Jan 22;395(3):627-42, EMBO J. 2009 Dec 2;28(23):3758-70.
E. Nollen	C. Dobson, M. Vendruscolo, T. Knowles Cambridge, UK	Analysis of early aggregation and toxicity in worms and test tubes. Student exchange, funded by ERC, Univ Cambridge, and Ubbo Emmius Fonds.

		Dietary interventions and cellular senescence
ERIBA		The project aims at investigating the induction of senescent cells in human and mouse tissues under dietary interventions.
M. Demaria B. Wang	L. Fontana Washington University, St Louis, USA	This project was initiated in June 2014. It has resulted in many data which will be soon sent out for publication and used for grant applications.

		Biomarkers of cellular senescence
ERIBA		The project aims at identifying better biomarkers for identification and isolation of senescent cells from human tissues.
M. Demaria	N. Sharpless University of North Carolina, Chapel Hill, USA	This project was initiated in May 2015. It has resulted in 1 published publication (Chang et al, Nat Med, 2016) and 1 submitted paper (Demaria et al, Can Discovery, 2016). It has the potential to attract investments from different pharma companies.

		Screening for calorie restriction mimetic drugs
ERIBA		We developed a reporter system for high-throughput screening to screen for small molecule compounds that suppress C/EBPβ-LIP expression and therefore may have calorie restriction mimetic properties.
C.F. Calkhoven	O. Pless Fraunhofer IME ScreeningPort Hamburg	The project was initiated in 2014. It resulted in a manuscript now in revision. A patent is filed for the reporter system and an identified drug. The project is funded by the city of Groningen and the city of Hamburg (110k).

		C/EBPβ determined changes in proteome and metabolome
ERIBA		To examine the role C/EBPβ-LAP and -LIP transcription factor isoforms in cancer metabolism we analyze changes in proteome and metabolome induced by LAP or LIP.
C.F. Calkhoven	S. Kempa Max Delbrück Center, Berlin	The project started in 2016. Manuscript in preparation.

		Generation of C/EBPβ mutant mouse models
ERIBA		We generated LIP-deficient (C/EBPβΔuORF) and conditional LIP-overexpressing mouse lines. Experiments included, metabolic phenotyping, motor-coordination phenotyping, lifespan determination, histology and pathology.
C.F. Calkhoven	Z-Q. Wang[1] J. von Maltzahn[1] J.P Tuckermann[2] A. de Bruin[3] Frits Lipmann Institute, Jena[1], University of Ulm[2] and University of Utrecht[3]	Projects started in 2011. It resulted in a published manuscript (EMBO Rep. 2015 Aug;16(8):1022-36), a second manuscript is submitted and a manuscript is in preparation.

		MYC-microRNA regulation in B cell lymphoma
ERIBA		The project examines the control of mTORC1-signaling by MYC through the regulation of microRNAs in the context of B cell lymphoma.
C.F. Calkhoven	Z-Q. Wang[1] C. Kosan[2] I. Petersen[2] Frits Lipmann Institute[1] and Friedrich Schiller University[2], Jena	The project was initiated in 2011. It resulted in a manuscript now in revision. The project was funded by the Deutsche Krebshilfe (250k), ERIBA and UMCG.

		Genome of the Netherlands project; Genome of ALS patients
ERIBA		Twin Res Hum Genet. 2013.16:1026-32. Eur J Hum Genet. 2014. 22:221-7; Genome Res. 2015. 25:792-801; Nat Genet. 2015. 47:822-6. Eur J Hum Genet. 2016. 24:263-70; Nat. Commun. 2016. 7:12989.
V. Guryev	Several national and international groups	Funded by BBMRI-NL.

		Study of transcriptome and epigenetic changes in ageing
ERIBA		Nucleic Acids Res. 2016. 44:1036-51.
V. Guryev T. de Jong	Yu. Moshkin, ICG, Novosibirsk Russia	

		Spatially resolved transcriptomics
ERIBA		Cell 159:662-75 (2014); Dev Cell. 36:36-49 (2016).
E. Berezikov	A. van Oudenaarden, J. Bakkers, Hubrecht Institute, Utrecht	Funded by ERIBA startup package.

		The ctenophore genome
ERIBA		Nature 510:109-14 (2014).
E. Berezikov	L. Moroz, University of Florida	Funded by ERIBA startup package.

		Karyotype polymorphism in Macrsotomum
ERIBA		PLoS One 11:e0164915 (2016).
E. Berezikov	N. Rubtsov, Institute of Cytology and Genetics, Novosibirsk	Funded by ERC starting grant.

		Identification of G4 function during transcription
ERIBA		
K. Paeschke	F. Brad Johnson, University of Pennsylvania, Philadelphia USA	Joint research project on G4 during transcription, manuscript under preparation. This work is funded by an DFG fellowship.

		RHAU function and importance at G4 motifs
ERIBA		
K. Paeschke	Markus Hafner, NIH, Bethesda, USA	Joint research project on RNA helicases, This collaboration is part of an DFG fellowship.

		In vivo characterization of the function of R64 peptide
ERIBA		
K. Paeschke	Bernt Gutte, ETH Zürich	Joint research project on the peptide R64 and its in vivo contribution on changes in apoptosis, transcription, or telomere maintenance. This work is funded by the ERC.

		In vivo characterization and identification of G4 binding proteins
ERIBA		
K. Paeschke	A. Schlosser (Uni Würzburg) A. T Capra (Vanderbuilt University, USA)	Joint research project on the peptide R64 and its in vivo contribution on changes in apoptosis, transcription, or telomere maintenance. This work is funded by the ERC.

ERIBA		**Computational modelling of stem cell fate decisions**
J. Paridaen	C. Marr, Institute for Computational Biology, Munich	Funding applied for.

		Genome instability in early embryonic development
ERIBA		
P. Lansdorp D.Spierings	E.Kuijk E.Cuppen Center for Molecular Medicine, University of Utrecht	Joint research aimed to understand genome instability of early bovine embryogenesis initiated with damaged sperm cells.

		DNA repair in Fanconi Anemia
ERIBA		
P. Lansdorp D.Spierings	R. Eiges Shaare Zedek Medical Center Jerusalem, Israel	Joint research aimed to understand genome instability and DNA repair in human embryonic stem cells and induced pluripotent cells with defects the Fanconi DNA repair pathways. Ongoing.

		DNA repair in ATRX deficient human iPS cells
ERIBA		
P. Lansdorp D.Spierings	D. Hockemeyer T. Turkalo University of California, Berkeley, CA	Joint research aimed to understand genome instability and DNA repair in induced pluripotent cells with defects in ATRX, Rb, p53 and RTEL. Ongoing.

		Genome instability in induced pluripotent cells
ERIBA		
P. Lansdorp N.v.Wietmarschen	Y. Buganim R. Jaenisch MIT, Boston	Joint research aimed to understand genome instability in induced pluripotent stem cells as a function of reprogramming factors. Publication in Cell Stem Cell 15: 295-309, 2014.

		Genome instability in induced trophoblast stem cells
ERIBA		
P. Lansdorp N.v.Wietmarschen	Y. Buganim Hebrew Univ, Jerusalem, Israel	Joint research aimed to understand genome instability in induced pluripotent stem cells as a function of reprogramming factors. Publication in Cell Stem Cell 17: 543-556, 2015.

		Structural variation in the human genome
ERIBA		The goal of this large collaborative project (> 30 laboratories worldwide) is to study human genome variation in 3 selected families from different parts of the world using all currently available sequencing methods and approaches.
P. Lansdorp D. Spierings D. Porubsky	A.Sanders (EMBL, Heidelberg) and others of the 1000g-svgtrio consortium	In the course of this project it has become clear that Strand-seq has unique advantages to map polymorphic inversions and single nucleotide variations along the entire length of parental chromosomes.

ERIBA		**Chromatin changes involved in Type 2 diabetes remission**
M. Colomé-Tatché	Robert Schneider (Helmholtz Zentrum München and Ludwig-Maximilians-Universität München)	This project aims at elucidating the relationship between chromatin changes and remission of type 2 diabetes (T2D) in obese patients that have undergone sleeve gastrectomy. The patient samples will be provided by Dr. André Tchernof at the Endocrinology and nephrology department at McGuill University (Canada), while Robert Schneider's group will perform low input chromatin immunoprecipitation followed by next generation sequencing on them. This project is partially funded by a Helmholtz Young Investigators Group grant for M. Colomé-Tatché.

ERIBA		**Chromatin changes during oocyte maturation and early embryonic development**
M. Colomé-Tatché	Gavin Kelsey, Babraham Institute; University of Cambridge. United Kingdom	This project aims at elucidating what are the chromatin changes that occur during oocyte maturation and during early embryonic development in mice. To that end, we will study a set of different epigenetic marks during normal and abnormal development (with the use of knock-outs), using single cell bisulfite sequencing and low input chromatin immunoprecipitation followed by next generation sequencing. This project is partially funded by a Helmholtz Young Investigators Group grant.

ERIBA		**Epimutation rates**
M. Colomé-Tatché	Robert Schmitz, University of Georgia, Athens, USA and Frank Johannes, Population epigenetics and epigenomics, Technical University Munich, Germany	This project aims at studying how frequent changes in DNA methylation occur which are transmitted across generations. To that end, we use as a model the plant A. thaliana, because it offers a feasible experimental setup that allows for the tracking of epigenetic changes genome wide over several generations. This project was initiated in 2014 and has lead to one publication in Proc. Nat. Acad. Sci. USA (2015).

4. Infrastructure and key expertise

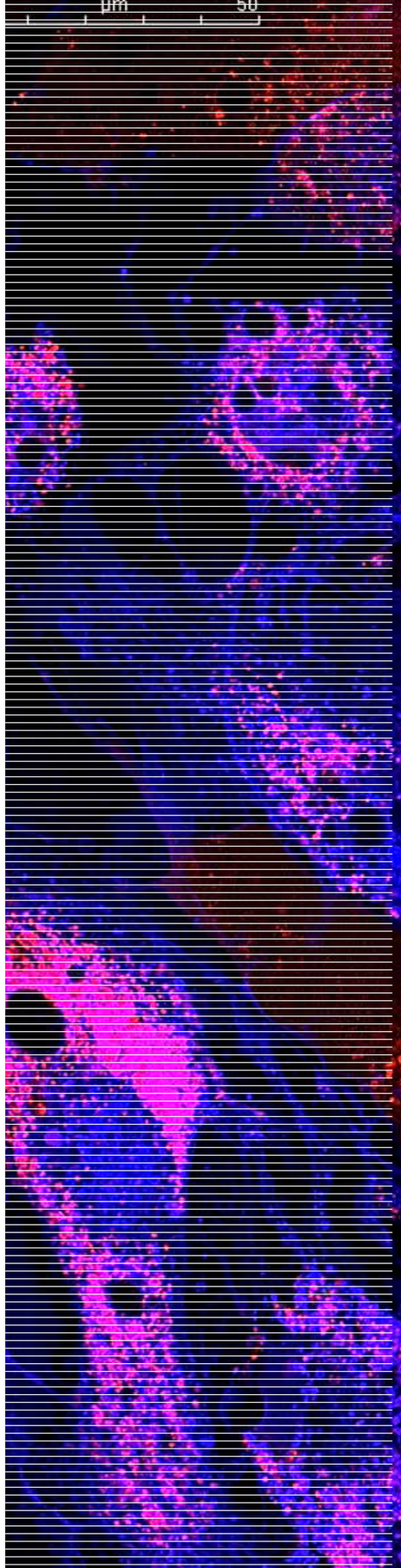
UMCG Facilities

ERIBA researchers have access to all the shared facilities that are present on the UMCG Campus. These include the Central Animal Facility, which houses all experimental vertebrate models, including fish and mice. The Central Animal Facility also is home for the Mouse Clinic for Cancer and Ageing, described in more detail further in this chapter.

Although ERIBA laboratories are equipped with many state-of-the-art microscopes, more advanced imaging resources are available at the UMCG Microscopy and Imaging Center. The UMIC offers training and access to advanced microscopes and image processing software to researchers of the UMCG and to external users.

On its first floor ERIBA offers a small laboratory for flowcytometry, where single sorting and sophisticated multi color cell analysis is possible. However, in addition ERIBA scientists have full access to the UMCG Central Flowcytometry Unit, where many other machines are present. ERIBA has supported this CFU by equipping the CFU with a MoFlow Astrios (purchased through a Netherlands Institute for Regenerative Medicine grant awarded to G. de Haan and RC Coppes), and by providing salary support for a part-time operator based at the CFU.

The 6th floor of the ERIBA building is home to the Facility for Proteomics and Metabolomics, which contains a range of mass spectrometers, and constitutes a shared facility between the UMCG and the Faculty of Mathematics and Natural Sciences.



Fish Expertise

The Central Animal Facility (CDP) of the University Medical Centre Groningen is one of the 13 Academic Experimental Animal Institutions in The Netherlands. The Central Animal Facility (CDP) is a facility of the UMCG where all animal experimentation is conducted. The CDP supports and facilitates research and education projects involving experimental animals.

The mission statement of the Central Animal Facility of the UMCG is:
"Professionally facilitate and support animal experimentation with optimal animal welfare control ."

In 2016, a fish unit was establishes within the CDP. This unit offers state-of-the-art housing for killifish *(Nothobranchius furzeri)* and zebrafish *(Danio rerio)*.

Key Expertise

- Breeding and care taking of rodents and fish, biotechnical support, micro-surgical support, imaging support, animal welfare monitoring.

SERVICES

- Dedicated animal care-takers trained in breeding, care and health services in housing small fish species.
- Dedicated microinjection and fluorescence microscopy setup for microinjection, analysis and manipulation of zebrafish and killifish embryos.

WHO

Catriene Thuring · Animal Welfare Officer, Deputy Head CDP
Judith Paridaen · ERIBA PI (zebrafish)
Eugene Berezikov · ERIBA PI (killifish)
Alex Kluppel · Manager CDP

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iPSC CRISPR Facility

The iPSC CRISPR Facility is a newly opened expertise centre at the ERIBA. It offers services for the generation of induced pluripotent stem cells (IPSCs) and genome editing using CRISP-Cas9 to both academic and non-academic researchers. The facility assists at three different levels, 1) by providing technical and intellectual advice, 2) by providing hands-on training and 3) by actually performing iPSC and CRISPR-related experiments.

The facility can generate iPSCs from human and murine somatic cells derived from multiple sources (e.g. skin biopsies or urine). iPSC clones are fully characterized with the option to introduce genetic changes using CRISPR/Cas9 technology. The facility also advises on and performs CRISPR/Cas9-genome editing of many other cell types/lines in order to knockout or tag a gene or alter the expression of a gene without manipulation of the genome. The facility will monitor the rapidly evolving field of iPSC and CRISPR technologies in order to incorporate and implement the latest protocols available, but also invest technology development. This is further aided through extensive collaboration of the facility with various other iPSC- and CRISPR-labs, both locally and (inter)nationally. Enduring state of the art protocols and scientific excellence are ensured by the facility's scientific advisory board that consists of local PIs with relevant expertise, and who regularly meet with the facility's personnel.

WHO

Floris Foijer · Coordinator IPSC/CRISPR facility
Bart van de Sluis · Coordinator CRISPR mice
Stefan Juranek · Senior Postdoctoral Fellow
Daniël Warmerdam · Senior Postdoctoral Fellow
Mathilde Broekhuis · Technician
Eslie Huizinga · Technician
Marike Smit · Technician

KEY EXPERTISE AND SERVICES

The IPSC/CRISPR facility generates, characterizes, and biobanks iPS cell lines from various (primary) sources. The combined expertise on iPSC and CRISPR allows the facility to support researchers during any stage of their iPSC and/or CRISPR project, through advice, training, or experimental help. The facility's basic services include:

Generation of iPSCs
- Isolation of somatic cells from different sources
- Reprogramming of somatic cells into iPS cells
- Biobanking of iPS cells

Characterization of iPSCs
- Pluripotency markers gene expression (qPCR, NGS, or immunofluorescence)
- Validation of differentiation potential (embryoid body formation and outgrowth into different lineages, checked by qPCR, NGS, or immunofluorescence)
- Proof of pluripotency potential by teratome formation in athymic mice
- Karyotyping by metaphase spreads or single cell sequencing

CRISPR Cas9-mediated genome editing services
- Gene knock-out
- Gene tagging/ knock-in
- Gene alterations (mutations)
- Gene expression regulation (transcriptional and epigenetic)
- Genetic screens using human or mouse CRISPR libraries
- Visualization of genomic loci

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Mouse Clinic for Ageing and Cancer (MCCA)

The Netherlands Cancer Institute (NKI) and the European Research Institute for the Biology of Ageing (ERIBA) have established a Mouse Clinic for Cancer and Ageing research (MCCA) aiming at accelerating the development of genetically engineered mouse models (GEMMs) of human cancer and ageing syndromes.

Key Expertise

- A Transgenic facility for efficient derivation, genetic modification and distribution of embryonic stem cell (ESC) lines from GEMMs, and for production of ESC-derived mice (@NKI).
- A Mouse Cancer Clinic for preclinical intervention studies and imaging of cancer growth and therapy response in advanced mouse models of human cancer (@NKI).
- An Ageing and Phenotyping Facility for controlled ageing and phenotyping studies in different inbred mouse strains and GEMMs, and for creating a centralized biobank of frozen mouse tissues for ageing research (@ERIBA).

WHO

Ivo Huijbers · Project coordinator
(Transgenic Facility-NKI)
Marieke van de Ven · Project Coordinator
(Mouse Cancer Clinic-NKI)
Alex Kluppel · Project coordinator
(Ageing and Phenotyping facility-ERIBA)
Ronald van Os · Scientific coordinator
(Ageing and Phenotyping facility-ERIBA)

FACILITIES

Transgenic Facility
This facility provides typical services related to the generation and cryopreservation of mutant mouse strains, such as construct design, Embryonic Stem Cell (ESC) culture, micro-injection and sperm cryopreservation. Additionally, a new pipeline has been developed for the fast and easy modification of existing Genetically Engineered Mouse Models (GEMMs), called the GEMM-ESC strategy

Mouse Cancer Clinic
The goal of the Mouse Cancer Clinic is to use advanced mouse models as surrogate cancer patients to identify and validate targets that can be exploited by anti-cancer therapy. Various approaches to treat cancer with classical chemotherapy, targeted inhibitors, immunotherapy, radiotherapy or combinations thereof are ongoing. Special emphasis is given to target the clinical handicap of therapy escape.

Ageing and Phenotyping Facility
The Ageing and Phenotyping facility, incorporated within the Central Animal Facility on the UMCG campus, can accommodate 10,000 mice that are held in Individually Ventilated Cages (IVC racks) in several holding rooms. The facility is split into two sections, a double barrier part where life-span studies will be carried out and multiple mouse strains will be aged to a maximum of 24 months. A procedure room is available in this section where simple experiments can be carried out. Experiments requiring interventions by the researchers will be carried out in a special section with a single barrier. A large variety of tissues from differentially aged mice of multiple mouse strains is available for external collaborators

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Seahorse XF96 Analyser Expertise

The Seahorse expertise is offered by the Calkhoven group and uses the XF96 Extracellular Flux Analyser from Seahorse Agilent Technologies. The Seahorse XF96 Analyser measures the oxygen consumption rate (OCR) and extracellular acidification rate (ECAR) of live cells in a 96 multi-well plate to examine metabolic cellular functions such as mitochondrial respiration and glycolysis. The instrument can perform compound addition and mixing, label-free detection, and automatic calculation of OCR and ECAR in real time.

WHO

Cor Calkhoven · Coordinator
Christine Müller · Coordinator
Tobias Ackermann · Doctoral student
Gertrud Kortman · Technician

KEY EXPERTISE AND SERVICES

The team offers introduction to the technique by one of the Calkhoven group members. Usage of the Seahorse is subject to fees and must follow the rules that will be communicated to new users. The group coordinates workshops offered by Agilent Technologies.

Typical Seahorse analyses are:

Measurement of global metabolic flux
Measuring ECAR and OCR of cells gives insight into the active/favoured metabolic pathways the cell uses for energy production; glycolysis vs oxidative phosphorylation. Typically used to analyse if certain treatments, stimulations (e.g. growth factors) or genetic manipulation affect cellular metabolism.

Generation of metabolic flux profiles
The ability of measuring the metabolism in real-time and the possibility to inject drugs to the cells during the measurement enables to create metabolic profiles of single metabolic pathways (glycolysis and mitochondrial functions). This is usually performed after the initial global flux analysis to gain more insight into the molecular changes caused by a treatment or genetic manipulation.

Nutrients usage and dependence flux profiles
Different cell types use different nutrients for energy production. The injection of certain drugs combined with real-time metabolic flux analysis enables to determine the favoured nutrient source of the cell and its dependence on it. This is for example used to identify metabolic vulnerabilities of cancer cells, or changes in preferred nutrients after drug treatments or genetic manipulations.

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eriba.umcg.nl/groups/gene-regulation-in-ageing-and-age-related-diseases

Single Cell Sequencing Laboratory

Single Cell Sequencing is performed by the Lansdorp research group on a collaborative basis. Various single cell techniques are used to analyse e.g. transcripts in single cells, to study human genomic variation and to address questions about aneuploidy and genomic instability in normal human ageing and specific diseases.

Key Expertise

- Single-cell DNA strand sequencing (Strand-seq) identifies all parental DNA template strands inherited by daughter cells upon one cell division. This directional sequencing technique makes it possible to map sister chromatid exchange events at a very high resolution and to identify other genomic aberrations such as translocations or inversions, copy number variations (CNVs) and aneuploidy events or loss of heterozygosity. Additionally, Strand-seq can be used for refinement of references genomes and direct chromosome-length haplotyping.
- Single-cell whole genome sequencing (scWGS) is used for studying CNVs and aneuploidy events.

WHO

Peter Lansdorp · Head of the Facility
Diana Spierings · Single-Cell Sequencing Project Coordinator
Marianna Bevova · Illumina Sequencing Coordinator
Victor Guryev · Bioinformatic Support
Nancy Halsema · Techician
Karina Hoekstra · Wakker Technician
Jorn Staal · Technician

ACTIVITIES

Single-Cell Sorting

The facility has its own FACS-JAZZ sorter for which three technicians are trained to operate the system for single-cell sorting in either 96-wells or 384-wells plates.

Single-Cell Library Preparation

This facility prepares Strand-seq or scWGS libraries in a semi-automated manner on an Agilent Bravo liquid handling platform allowing 96 single cell libraries to be constructed simultaneously. Barcoded single cell libraries will be pooled and gel purified to remove adapter dimers and subsequently the quality and quantity of the library pools are assessed on a Bioanalyzer and Qubit fluorometer.

Sequencing

Sequencing of the single-cell sequencing libraries will be done in house on an Illumina HiSeq 2500 platform. Additionally, other libraries such as RNA-Seq or ChiP-seq libraries can be sequenced within our facility. Sequencing can be performed with single-read or paired-end protocols. We offer advise on what kind of sequencing runs suits your experiments best and can help with quality and quantity measurements of your libraries to obtain the best sequencing results.

Single-Cell Bioanalysis Toolkit

To analyze single-cell sequencing data, we have developed several software packages that are currently being assembled in a single-cell Bioanalysis Toolkit, which has a graphical user interface to facilitate analysis by non-bioinformaticians. It will contain the single cell sequencing analysis software packages BAIT and Breakpoint.R to map chromosome breakpoints, Invert.R to assess inversions and StrandPhase to generate whole genome haplotypes from Strand-seq data. The AneuFinder software will be implemented in the Toolkit to assess CNVs and aneuploidy events.

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5. Education

5. Education

Education at ERIBA is strongly connected with research. In all our laboratories we train prospective ageing researchers by exposing students to state-of-the art molecular tools, model organisms, technologies and approaches.

In the first five years of our existence, ERIBA has hosted a large number of students, originating from Groningen, other cities in the Netherlands, and many from abroad. Students enter our Institute at many different levels. This ranges from first year Medical students who do a small research elective, Bachelor students in Biomedical Sciences, Master students who spend research rotations, to doctoral student and MD doctoral students. We actively monitor where our doctoral students find employment after they have graduated, and take pride in the various awards and fellowships that they obtain. You will find a full report of the whereabouts of ERIBA Doctoral-graduates further in this report.

The Faculty of Medical Sciences and the Faculty of Mathematics and Natural sciences recognized early on that in the existing biomedical curriculum of the University of Groningen there was a lack of courses that were specifically focused on the (molecular) biology of ageing. Therefore, in the few years that we have been in existence, 'we have been involved in establishing the establishment of various undergraduate and graduate courses on ageing.

The courses we teach target different student communities, and therefore vary much in their nature and content. For example we offer small-group courses to medical students, in which they are exposed, often for the first time, to experimental research. This includes lectures on how model organisms such as yeast, worms, fish, and mice are used in ageing research and also includes some laboratory experience. As the (former) co-Director of ERIBA Gerald de Haan serves as Dean for the Learning Community Molecular Medicine, and lead a team to develop a new -English-taught- curriculum for the bachelor program of the Medical School.

For biomedical bachelor students we offer more extended research courses, in which students are embedded in one of our laboratories for four weeks to carry out a mini project. In collaboration with the Faculty of Natural Sciences we have been involved in the development of a track biology of aging for master students in Biomedical Sciences, which includes courses in which students learn the essentials of the molecular mechanisms that contribute to ageing. Master students are trained to digest and recapitulate seminars from invited speakers. Many biomedical sciences master students choose ERIBA for their science rotations, and spend five to six months in one of our research groups.

For doctoral students we established a course covering different bioinformatics approaches to use computational tools in data analysis and omics data integration. All ERIBA doctoral students are embedded in one of the various Research Institutes of the Graduate School of Medical Sciences Importantly, all rotation and doctoral students at ERIBA are taking part in weekly scientific seminars and attend invited lectures. Finally, we have developed the first Massive Open Online Course (MOOC) of the UMCG on molecular mechanisms of ageing, which has currently run for three times, attracting thousands of students globally.

Each of these above-mentioned courses is organized and 'owned' by one or two ERIBA PI's. In addition to these in-house courses, ERIBA PI's also contribute to multiple other educational programs at the RuG, elsewhere in the country and abroad.

We recognize the importance of education, and realize that education is more than just transferring knowledge. In our courses we hope to spark curiosity and want to share our enthusiasm for science in general, and ageing science specifically. Our educational activities therefore often do not comprise 'classical' classroom teaching. Rather, we engage into discussions with our students, who are expected to arrive prepared in the classroom.

In the next pages we provide a list of our major educational activities. While we believe that our collective educational effort has been substantial, we are keen to further develop a mature Biology of Ageing Research Track for students of our University, starting as a Bachelor and ending as doctoral student. We believe that a critical evaluation of the coherence of the multiple courses in which students in biomedical sciences at our University can presently enroll is warranted, and we are ready to contribute to such an evaluation.

Education Activities

ERIBA scientists are involved in many educational activities. Below we list a selection of our major contributions to teaching, which exclude a large number of individual lectures and undergraduate student internships.

2014 - present
"Model organisms in Ageing Research".
3 ECTS BSc Junior Scientific Master course, ~20 medical students per year.
Coordinator: **Floris Foijer**
Objectives: Expose medical students to basic research. Students receive lectures from (junior) scientists on how they use their model organisms of choice in their ageing-related research and discuss relevant papers. Furthermore, students spend some time in the laboratory, altogether giving them an impression of the 'live of a basic biologist'.

2012 - present
"Current Themes in Healthy Ageing". 5 ECTS MSc course ~ 20-35 students per year.
Coordinator: **Floris Foijer**
Objectives: How to get most out of scientific seminars. Biomedical Science students attend 7- scientific seminars and verbally report on content, scientific excellence and track records of the presenters. Course has been growing rapidly and now has > 30 students/year.

2014
Graduate School of Medical Sciences (GSMS) course on **"Data integration for biologists"**. One week course, 24 students (mostly doctoral students).
Coordinators: **Marianna Bevova and Victor Guryev**
Objectives: A one week introductory course on data analysis and integration for biologists who plan to explore and integrate large -omics-type data derived in several domains (DNA, RNA, proteins, etc).

2015
LUMC/GSMS NGS **"Next generation sequencing (NGS) data analysis"**. One week course for ~60 students.
Co-organizers: **Marianna Bevova and Victor Guryev and LUMC staff.**
Objectives: This course aims at doctoral students, postdoctoral fellows, and senior researchers who are interested in, planning, or already working with next-generation sequencing. We welcome researchers from both the genomics and bioinformatics fields. Currently available technologies as well as hard ware and software solutions are presented and discussed.

2015
Workshop **"Future perspectives in computational pan-genomics"**. One week workshop, 55 international researchers.
Co-organizer: **Victor Guryev**
Objectives: Pan genomics is research on larger collections of genomes from related individuals or cells, and not just single genomes. Exemplary collections represent human populations, ensembles of cancer and pathogen genomes ("viral quasispecies"). The idea of this workshop is to systematically bundle the so far often still separate efforts and to create maximum synergy among all researchers participating. The final goal of this workshop was to write a white paper that summarizes all those challenges and chances, and their overlap among the different fields and to publish it in a journal of high impact, as future guideline and roadmap for computational pan genomics research.

2016-present
Weekly seminars on **"Genome Biology Tools".**
Coordinators: **Victor Guryev and Leonid Bystrykh**
Objectives: Discuss data analysis and educate ERIBA BSc, MSc and doctoral students on genome biology tools.

2014-present
"Molecular Biology of Ageing and Age related Disease". 5 ECTS MSc course ~ 20-35 biomedical students per year.
Coordinator: **Liesbeth Veenhoff**
Objectives: In this course we focus on the molecular and cellular mechanisms by which tissue and organ function deteriorate and homeostasis fails, resulting in ageing and age related disease. We present the model systems and experimental strategies that are used in ageing research. This course will be supported by a team of specialists in different fields of ageing that will provide lectures and reading material. The course will be further supported by materials from an online course "Why do we age? The molecular mechanisms of ageing". The course not only gives an overview of the research field of ageing but also teaches scientific writing, active listening and giving feedback to peers. The course unit is compulsory for the ageing track and is an elective in the other tracks of the programs.

2015-present
"Molecular and Genetic Age Research at ERIBA". six weeks practical research course, 10 ECTS, 18 Bsc biomedical students.
Coordinator: **Cor Calkhoven**
Objectives: "Hands-on" research course for biomedical students. Research topics cover a broad range of techniques and model systems related to ageing, lifespan and age-related diseases. Topics may involve (stem) cells, yeast, worms, mice, and cover the biological processes of signal transduction, transcription, translation, post-translational modification, protein homeostasis, energy metabolism, chromosome biology, genetics and epigenetics. Students should choose a first choice laboratory and a second choice laboratory research which are i) Molecular Biology of Ageing course and ii) Current themes in Health Ageing.

Ongoing
"Course on Modern Techniques". 6-week course within the MPDI Topmaster Program. 15-30 students are enrolled each year.
Coordinator: **Deelman/Melgert**
Objectives: In this course students are taught how to identify a research question and how to use different research methods to solve research questions. Two of the six weeks are coordinated by Eriba PIs (Chang, Nollen, Veenhoff). When ERIBA started and new model organisms were introduced (e.g. *Macrostomum*, yeast) new lectures and practical courses have been added and are given by ERIBA PIs.

2013-present
Learning Community Molecular Medicine. Bachelor program for medicine students.
Coordinator: **Gerald de Haan**
In 2014 a new bachelor curriculum for medicine students was implemented, referred to as G20202. Gerald de Haan lead a team that developed the -english taught- curriculum for ~95 students each year that enroll in the Molecular Medicine track.

On demand
"Seahorse XF workshop". Seahorse Seminar and Free Workshop,presented by Seahorse Biosciences (Agilent Technology).
Coordinator: **Cor Calkhoven**

2015-present
MOOC (Massive Online Course) **"Why do we age? The molecular mechanisms of ageing"** (www.futurelearn.comwww.futurelearn.com). 6-weeks free online course, three editions so far, ~2500 learners for each round.
Coordinator: **Marianna Bevova**
Objectives: The aim of this first on-line course of the UMCG is to provide an overview of currently existing theories and mechanisms related to ageing. During the course the problems and questions scientists face when they investigate the biology of ageing are discussed. Additionally an overview is given on experimental approaches and model organisms used in ageing research. The course will be translated in Ukrainian in 2017.

2012-present
Specialization Track on the Biology of Ageing. Master students in Biomedical Sciences (FWN).
Coordinator: **Ellen Nollen**
Objectives: For the track, a combination of existing courses has been selected and two new courses have been developed that are important to train biology of ageing

6. Business Development

6. Business Development

ERIBA appointed a dedicated business developer, dr. Craig Grove, to connect scientific discoveries made by ERIBA researchers with industrial partners. Craig's primary role is to actively seek opportunities to liaise with existing companies and develop start-ups, and to identify intellectual property, aid in preparing and writing patent applications, which can support such opportunities. Craig is also a team member of the UMCG Center for Development and Innovation (CDI).

To ensure legal matters surrounding Intellectual Property are dealt with in a fast an accurate manner, an Intellectual Property pipeline was set up for ERIBA in the opening phases of its existence, in collaboration with the UMCG legal office. Such pipeline has facilitated researchers in the assessment, communication and execution of MTAs, NDA, CDAs etc, in a fast and professional manner.

During ERIBAs first 4 years, scientific research has resulted in discoveries that will potentially translate to society. A number of drug targets, biomarkers, stem cell therapies, model systems and technologies have been identified, evaluated and, in many cases, continually developed. Nevertheless, one of the challenges ERIBA faced was a lack of expertise and infrastructure in translating drug targets by generating robust screening assays and accessing compound libraries to screen for drug candidates. To overcome this challenge ERIBA formed a strategic partnership with Fraunhofer IME Screening Port, Hamburg. This has strengthened the institutes translational capacity in drug discovery and biomarker development, with the first compound already identified within the framework of the partnership. The drug candidate, identified by the Calkhoven Laboratory, can mimic calorie restriction and potentially extend life-span, decrease body mass and reduce the risk of cancer, cardiovascular diseases and diabetes. ERIBA is building an IPR position on this compound to enable further development and attract adequate funding.

Further validation of potential drug targets from ERIBA is continuous. The Nollen Laboratory continues to validate TDO and SERF as drug targets to treat neurodegenerative diseases as well as a novel unpublished drug target that ERIBA is currently securing an IPR position on. The de Haan Laboratory has also discovered a new method to mobilize stem cells from peripheral blood that is anticipated to increase the efficiency of bone marrow transplants in leukaemia patients. The invention relates to a specific microRNA that renders hematopoietic stem cells prone to leave the bone marrow, mobilizing them to the peripheral blood. They have identified downstream targets of this microRNA, of which ERIBA is securing an IPR position on.

In collaboration with the UMCG Department of Cardiology, the Berezikov Laboratory discovered a novel microRNA biomarker array used to predict the likelihood of a patient developing Acute Heart Failure. ERIBA is currently securing an IPR position on this biomarker in parallel with its continuous development in collaboration with the clinic. Other biomarkers that are currently being validated include a number of potential indicators of biological age.

ERIBA continues to build on its patent portfolio and identify strategic partners that will bring its knowledge further to society. Significant progress has been made over the past four years in the identification, protection and development of Intellectual Property Rights. This progress has resulted in increasing interactions with industrial partners and an increased awareness of the research potential stemming from the Institute .

7. Funding

7. Funding

The establishment of ERIBA was made possible by financial contributions of in total €50M, which was secured from several sources, indicated below. The construction of the building was made possible by a contribution of €15M from the University of Groningen. The UMCG contribution amounted to ~ €15M, of which €10.2M consisted of 'in kind' support.

1. Start-up Funding (2012-2016)	
Building	€ 15.000.000
Equipment	€ 9.700.000
Packages	€ 22.700.000
Exploitation	€ 2.300.000
Total	**€ 49.700.000**

2. Financing	
National Public Sector	
SNN	€ 6.900.000
Europees Fonds voor Regionale Ontwikkeling	€ 100.000
Regional Economic Programme	€ 4.000.000
Ministry of Economic Affairs	€ 4.000.000
Province of Groningen (Co-financing)	€ 2.000.000
National Private Sector	
Naober Foundation/SKOG	€ 2.500.000
UMCG/RuG:	
Personnel (UMCG)	€ 10.200.000
Building (RuG)	€ 15.000.000
Endowed Chair (UMCG/RuG)	€ 5.000.000
Subtotal	€ 30.200.000
Total	**€ 49.700.000**

3. Research Grants and Funding

The Research Development Office of ERIBA (RDO) was created in 2012 to support scientists in raising funds to pursue their scientific activities, which is crucial to boost their careers at any point, particularly in an early stage. The RDO is managed through the following functional areas:

1. Funding strategy
2. Research Funding Administration and Management
3. Intellectual Property
4. Business Development

A specialized team of professionals provides support to ERIBA scientists on a daily basis and builds the necessary relations with the different offices of the UMCG engaged with grants and funding. The team members are Helena Rico, Project Manager (funding opportunities, international cooperation and communication), Catarina Rodrigues, Project Manager (funding opportunities, legal affairs and ethics), Craig Grove, TTO, (business development and valorization) and Klaas Martens, Financial Officer (finances, reporting and monitoring). With ERIBA's scientific goals at heart, the RDO attempts to remove most of the bureaucratic, managerial, legal and financial load from scientists and students so that they can focus on their research.

The next pages summarize the collective effort of ERIBA PIs in setting up and putting forward a wide variety of research proposals, which have been submitted in the past six years to various public and private funding bodies. The total amount of external funding that has been secured by ERIBA PIs was 27,6M M Euro. In 2011 we secured 1,4 M Euro, in 2012 17,8M Euro, in 2013 1,4M Euro, in 2014 0,64M Euro, in 2015 1,83M Euro, and in 2016 4,5M Euro (with several grants still pending).

Between 2011 and 2016 a total number of 97 grants was submitted. As of December 1, 2016, 33 of these grants were awarded, 52 grants were not funded, and 12 grants are pending. The ERIBA RDO will continue to support research applications with the objective of obtaining more funding in the coming years.

Research proposals submitted in the period 2011-2016

2011

PI	Role	Grant	Title	Budget	Status
Chang	Applicant	NWO VIDI	Characterizing replicative senescence and its bypass via telomerase-independent mechanisms	€ 800.000	Submitted
	Applicant	HFSP Career Development Award	Characterizing replicative senescence and its bypass via telomerase-independent mechanisms	$US 300.000	Submitted
Foijer	Applicant	Marie Curie Integration Grant	Consequences of genomic instability for epidermal stem cells and cancer	€ 100.000	Submitted
Nollen	Applicant	ERC Starting Grant	Protein damage control: regulation of toxic protein aggregation in ageing-associated neurodegenerative diseases	€ 1.450.249	Awarded

2012

PI	Role	Grant	Title	Budget	Status
Berezikov	Applicant	ERC Starting Grant	Rejuvenation through regeneration: stem cells and ageing in the flatworm *Macrostomum lignano*	€ 1.500.000	Awarded
Chang	Applicant	NWO ALW Open	Characterizing the effect of dGTP on telomerase activity	€ 250.000	Submitted
	Applicant	Marie Curie Integration Grant	Characterizing DNA recombination at telomeres	€ 100.000	Submitted
	Applicant	NWO VIDI	Protecting the ends: characterizing the role of recombination at telomeres	€ 800.000	Awarded
de Haan	Main Applicant	Marie Curie Initial Training Networks	MARie CuRie AGEing Network - MARRIAGE	€ 490.665	Awarded
de Haan	Co-Applicant	Mouse Clinic for Cancer and Ageing Research - MCCA	NWO	€ 4.475.000	Awarded
Foijer	Applicant	KWF	Mouse models for aneuploid T-cell lymphoma to study consequences of chromosomal instability	€ 553.500	Awarded
	Applicant	Marie Curie Integration Grant	Consequences of aneuploidy in mouse epidermis: mechanisms of stem cell depletion, premature ageing and malignant transformation	€ 100.000	Submitted
	Applicant	Nijbakker-Morra Foundation	Causes and consequences of aneuploidy in paediatric AML	€ 17.600	Submitted
Lansdorp	Main Applicant	ERC Advanced Grant	Role of telomeres and stem cells in ageing	€ 2.500.000	Awarded
Lansdorp (co-applicants: de Haan, Berezikov)	Main Applicant	Skoltech-Skolkovo Institute of Science and Technology	Skolkova Center for Stem Cell Research (seser)	€ 5.859.625	Awarded
Lansdorp (co-applicants: de Haan, Guryev, Berezikov, Chang)	Main Applicant	NWO	The Centre for Integrative Ageing Studies	€ 19.574.000	Submitted
Mata-Cabana (host supervisor: Nollen)	Applicant	FP7-MC-IEF	Cellular protein damage control: interactomic analyses of MOAG-4 in *C. elegans* - AGGREGATION	€ 175.974	Awarded

2013

PI	Role	Grant	Title	Budget	Status
Berezikov	Applicant	Netherlands Genomics Initiative (NGI) Horizon Programme Valorisation Project Grant	Novel Application of an RNA helicase for amplification of hematopoietic stem cells in vitro	€ 47.327	Awarded
Chang	Applicant	NWO ALW Open	Genome-wide high resolution analysis of DNA recombination events in single cells	€ 250.000	Submitted
Colomé-Tatché	Applicant	NWO Meervoud	Unravelling the combinatorial epigenic code during ageing	€ 221.101	Awarded
Foijer	Co-Applicant	Marie Curie Initial Training Networks	The impact of chromosomal instability on health: Molecular causes and consequences of aneuploidy.	€ 376.758	Awarded
Foijer, Bruggeman	Main Applicant	UMCG Cancer Research Fund	Modeling aneuploid medulloblastoma	€ 11.000	Awarded
Lansdorp, de Haan, Guryev, Berezikov	Co-applicants (Main applicant: Hoeijmakers)	NWO Zwaartekracht	Netherlands Institute of Healthy Ageing Research - NIHAR	€ 15.753.000	Submitted
Nollen	Applicant	Gooische Groningers	The link between ageing and dementia	€ 500.000	Awarded
	Applicant	ZonMw - Joint Programme - Neurodegener-ative Disease	Tryptophan metabolism as a regulator of protein toxicity in neurodegenerative diseases	€ 4.996.544	Submitted
Veenhoff	Applicant	NWO ECHO	Ageing and the structure and function	€ 260.000	Awarded
	Applicant	ERC Consolidator	Traffic to the inner nuclear membrane: unravelling age-related changes in nuclear envelope function.	€ 2.000.000	Submitted

2014

PI	Role	Grant	Title	Budget	Status
Berezikov/ Grudniewska	Applicant	Jan Kornelis de Cock-Stichting	Characterisation of mitochondriae in the emerging model *Macrostomum lignano*	€ 4.000	Awarded
Belderbos (co-applicant: de Haan)	Main Applicant	KWF	Clonality of normal and leukemic human hematopolesis	€ 50.000	Awarded
Chang	Co-applicant	COST	Nucleotide pool imbalance in health and disease – NPHD)	----	Submitted
Calkhoven, Foijer	Main Applicant	UMCG Cancer Research Fund	Optimizing transfection of primary (cancer) cells to tag or target gene by CRISPR/Cas9 technology	€ 45.000	Submitted
de Haan	Applicant	KWF	The function and therapeutic targeting of Polycomb CBX proteins in leukemia	€ 572.500	Awarded
	Co-Applicant	H2020 - CSA	European consortium for communicating stem cell research	n.a.	Awarded
Foijer	Applicant	ERC Starting Grant	A life full of CIN, the implications of aneuploidy on cancer and ageing.	€ 1.500.000	Submitted
	Applicant	NWO VIDI	Analysing the in vivo molecular responses to chromosomal instability to explore therapeutic potential	€ 800.000	Submitted
	Applicant	KWF Cancer Career Award	Monitoring in vivo consequences of chromosomal instability to resolve therapeutic potential	€ 450.000	Submitted
Foijer, Bruggeman	Main Applicant	STOPHERSEN-TUMOREN	Modeling medulloblastoma subgroups in the mouse using chromosomal instability as a driver	€ 93.600	Submitted
Foijer/Bakker	Applicant	Jan Kornelis de Cock-Stichting	Opzetten van een muismodel voor aneuploid medulloblastoom	€ 4.000	Awarded
Guryev	Applicant	ERC - Consolidator	Prevalence and effect of low-frequency structural genome variants in the general human population-Rare SV	€ 2.000.000	Submitted
Lansdorp	Applicant	ERC - Proof of Concept	SCOOP-Single Cell genOmics Open Platform	€ 150.000	Submitted
	Co-Applicant	Health Programme - PHC1	Eureca - European Research Counteracting Ageing	€ 402.237	Submitted
Nollen	Co-Applicant	Health Programme - PHC1 Rejuvenation	The Mechanism Regulating Ageing and Rejuvenation	€ 583.047	Submitted
Nollen/de Haan	Applicant	Marie Curie Cofund	Doctoral Programme on the Biology of Ageing	€ 1.464.960	Submitted
Veenhoff	Applicant	ERC - Consolidator Grant	Nuclear transport and cellular ageing	€ 2.000.000	Submitted
	Applicant	VICI Scheme	Nuclear transport and cellular ageing	€ 1.500.000	Submitted

2015

PI	Role	Grant	Title	Budget	Status
Bevova	Co-Applicant	H2020-SEAC-2015-1	Authentic research in STEM for the young generation in Europe - STEM4U	€ 130.789	Submitted
Berezikov	Applicant	NWO VICI	Molecular basis of the highly efficient DNA damage control in the flatworm *Macrostomum lignano*: links to cancer, regeneration and ageing	€ 1.500.000	Submitted
Belderbos (co-applicant: de Haan)	Main Applicant	KWF – Bas Mulder Award	Predicting clonal chemoresistance in acute lymphoblastic leukemia using in vivo barcoding	€ 513.276	Awarded
Chang	Applicant	Vellux Stiftung	Single cell analysis of protein abundance and localization changes during yeast replicative ageing	€ 482.167	Submitted
de Haan	Applicant	NWO	Functional expansion and Megakaryocyte differentiation of hematopoietic stem cells	€ 346.000	Awarded
de Haan	Applicant	ERC Advanced Grant	Genetic and epigenetic pathways controlling hematopoietic Stem cell Ageing - StAge	€ 2.499.982	Submitted
de Haan, Calkhoven (Main applicant: Rasmussen)	Co-applicants	H2020-MSCA-ITN-2016	MetabolAge	€ 616.250	Submitted
Foijer	Applicant	KWF	Identifying molecular mechanisms to better treatment of aneuploid cancer	€ 564.900	Awarded
	Applicant	H2020-MSCA-ITN-2015	Does aneuploidy trigger ageing? Investigating the relationship between Ageing and Genomic Instability - AGIN	€ 3.302.288	Submitted
	Applicant	NWO VIDI	CINister problems, CINister solutions: understanding and exploting the molecular responses to aneuploidy to develop new cancer therapies	€ 800.000	Submitted
Foijer, Bruggeman	Main Applicant	STOPHERSEN-TUMOREN	Understanding the role of aneuploidy in medulloblastoma	€ 28.598	Submitted
Guryev	Co-Applicant	LongFonds	Proteogenomics, the missing link to identify causal networks involved in COPD development	€ 750.000	Submitted
Lansdorp	Co-Applicant	H2020-MSCA-ITN-2015	Quadruplex Selective ligands as potential drugs for cancer, aids and als - QUASELTNET	€ 255.374	Submitted
Nollen	Applicant	Weston Brain Institute	Inhibitors of O2-AA enzymes for age-related neurodegenerative diseases	€ 200.000	Submitted
Nollen	Applicant	EMBO Young Investigator Award	Cellular protein damage control: regulation of age-related protein aggregation and toxicity	€ 45.000	Awarded
Nollen/de Haan	Applicant	EU - COFUND	An interdisciplinary, international and inter-sectorial Doctoral Programme in the Biology of Ageing - GRaduAge	€ 1.464.960	Submitted
Nollen/Neto Marchante	Applicant	H2020-MSCA-IF-2015	Studies of amyloid propagation in the nematode *C. elegans* - STAMP	€ 165.598	Submitted
Paeschke	Applicant	ERC Starting Grant	G-quadruplex DNA Structures and Genome Stability	€ 1.531.625	Awarded (*)
Paridaen	Applicant	NWO VIDI	The regulation of stem cell differentiation at the single cell level	€ 800.000	Submitted
	Applicant	ERC Starting Grant	StemCellDecisions. Stem cell decision-making: from individual stem cell biology to predictable lineage outcomes	€ 1.500.000	Submitted
Veenhoff	Applicant	NWO ALW Open	A mother's sacrifice: asymmetric inheritance of ageing factors	€ 260.351	Awarded
	Applicant	Aspasia (coupled to VICI grant application of 2014)	Nuclear transport and cellular ageing	€ 150.000	Awarded

(*) Grant awarded while the applicant was a Group Leader at the University of Würzburg, Würzburg, Germany. The grant was transferred to ERIBA in 2016.

2016

PI	Role	Grant	Title	Budget	Status
Berezikov	Applicant	KWF	Molecular basis of the highly efficient DNA damage control in the flatworm *Macrostomum lignano*	€ 149.940	Pending
Berezikov/ Mouton	Applicants	ZonMw Off Road	Eliminating Flukes: screening for drugs using free living flatworms	€ 100.000	Submitted
Calkhoven	Applicant	KWF	Oncogenic functions of the transcription factor C/EBP- in breast cancer	€ 670.000	Awarded
	Applicant	Stichting Zeldzame Ziekten Fonds	Shwachman–Bodian–Diamond syndrome (SBDS)	€ 66.000	Pending
	Applicant	City of Hamburg and City of Groningen	A Genetic Switch for Healthy Ageing - A drug discovery campaign for novel calorie restriction mimetic and anti-cancer drugs	€ 110.000	Awarded
	Applicant	Velux Stiftung	Extending the time window for healthy ageing	€ 570.000	Submitted
Calkhoven/ Guryev	Applicants	NWO – Complexity in Health and Nutrition 2016	Exploiting the C/EBP-centered regulatory network that controls nutrition-mediated health effects	(Preliminary Application)	Pending
Chang	Applicant	NWO ALW Open	Studying the maintenance of genome stability during yeast replicative ageing	€ 250.000	Submitted
	Applicant	NWO ALW Open	Analysing genome instability by measuring sister chromatid events genome-wide using single-cell sequencing	€ 250.000	Submitted
Chang/Veenhoff	Applicants	KWF	Analysing genome instability, a hallmark of cancer, by measuring sister chrotmatid exchange events genome-wide using single cell sequencing	€ 618.155	Submitted
de Haan	Co-Applicant	H2020-INFRADEV-2016-2017	Towards enduring mouse resources and services advancing research into human health and disease - INFRAFRONTIER2020	€ 20.800	Awarded
de Haan, Foijer, Lansdorp	Applicants	NWO TOP Grant	Reprogramming hematopoietic progenitors to generate transplantable stem cells	€ 669.500	Awarded
de Haan, Nollen, Lansdorp, Veenhoff, Sibon	Co-Applicants (Main applicant: Hoeijmakers)	Zwaartekracht	Netherlands Institute of Healthy Ageing Research - NIHAR	€ 23.034.000	Submitted
Demaria	Applicant	NWO Building Blocks of Life	Development of multicellular 3D skin cultures for the study of human ageing and age-related pathologies.	€ 493.774	Submitted
	Applicant	NWO ALW Open	Molecular pattern and biological significance of sub-populations of senescent cells	€ 250.000	Pending
	Applicant	ERC Starting Grant	IMMUNSEN: Accumulation of deleterious senescent cells in immunosuppressed environments	€ 1.496.189	Pending
	Applicant	KWF	Clearance of UV-induced senescent cells as strategy to delay melanoma progression	€ 614.445	Submitted
Foijer	Applicant	H2020-MSCA-ITN-2016	Does aneuploidy trigger ageing? Investigating the relationship between Ageing and Genomic Instability	€ 3.793.891	Submitted
Foijer, Warmerdam	Applicant	UMCG Cancer Research Fund	Precise creation and detection of genome editing events in human stem cells	€ 45.000	Awarded
Guryev	Applicant	NWO VICI	Personalized proteogenomics approach to study human diseases	€ 1.500.000	Submitted
	Applicant	KNAW PSA	A”Silk”Road”to”precision”medicine:”multi5omics”approach”to”understand”roles”of”genetic”and”environmental”factors”in”lung”diseases	€ 1.518.00	Submitted
	Co-Applicant	LongFonds	A novel proteogenomics approach in COPD to identify causal molecular networks and unique patient specific protein forms underlying COPD development	€ 750.000	Submitted

PI	Role	Grant	Title	Budget	Status
Guryev	Co-Applicant	KWF	Unravelling the different stages of cervical carcinogenesis with proteogenomics	€ 1.374.500	Submitted
	Co-Applicant	KWF	Search for specific autoantibodies for diagnosis of lung carcinoma at baseline	€ 793.800	Submitted
	Co-Applicant	Noordelijke Cara Stichting	Gene expression analysis of IL33 mediated effects on TH2 lymphocytes in asthma	€ 5.000	Awarded
Lansdorp	Co-Applicant	H2020-MSCA-ITN-2016	G4TooTher G-Quadruplex Tools and Therapeutics	€ 255.374	Submitted
Nollen	Applicant	NWO VICI	Regulators of protein toxicity in ageing and age-related diseases	€ 1.500.000	Submitted
	Applicant	The Michael J. Fox Foundation	Exploring SERF inhibition as therapeutic strategy to suppress alpha-synuclein proteotoxicity in disease	Pre-proposal	Pending
	Applicant	CORBEL Track 2	Exploring SERF inhibition as therapeutic strategy to suppress proteotoxicity in age-related disease	Pre-Proposal	Pending
Nollen/ Koopman	Applicants	Frick Foundation	Disentangling the genetic networks underlying TDP-43 toxicity: screening and modelling in *Caenorhabditis elegans*	€ 100.968	Pending
Paeschke	Applicant	NWO VIDI	RNA G-quadruplex structures and their impact on translational efficiency.	€ 800.000	Pending
Paridaen	Applicant	NWO VIDI	The regulation of stem cell differentiation at the single cell-level	€ 800.000	Pending
Veenhoff	Co-applicant	NWO Building Blocks of Life	Unravelling the molecular mechanism of impaired nuclear transport in ALS	€ 749.922	Awarded
	Applicant	NWO VICI	Nuclear Pore Complex Function in Ageing and Disease	€ 1.500.000	Pending
	Applicant	ERC Consolidator	PoreProblems: Nuclear Pore Complex Function in Ageing and Disease	€ 1.999.236	Submitted
Warmerdam	Applicant	NWO VIDI	Repairing repetitive DNA: when mistakes are easy to make	€ 800.000	Pending

Note: Proposals stated as “submitted” have not been awarded.

8. Public Outreach and Dissemination

8. Public Outreach and Dissemination

When visiting the ERIBA building, multiple things stand out to most people: the open and welcoming atmosphere, the beautifully constructed building and the ERIBA Science Hall. The Science Hall is a public space within the ERIBA building where visitors are welcome to get acquainted with ageing research in an entertaining way. Not just by the large number of interactive exhibits it features, but by the room itself as well: the Science Hall provides a clear view into one of the laboratories where scientists are working on their latest research.

This setup is the perfect example of what ERIBA is trying to reach with its dissemination activities. ERIBA does not just aim to inform or educate, but to effectively bring the general public closer to research. Through public events, activities for schools, tours and a website that contains news items on ERIBA's researchers and most recent research, ERIBA tries to connect with the world outside the academia.

Over the past five years, ERIBA has financially supported many engagement and communication activities and has financed a part time Outreach Officer, which demonstrates a consistent and serious commitment to science communication.

The most significant outreach activities are listed in the following pages and illustrate ERIBA communication strategy, which is meant to raise public awareness of the work performed by the Institute, at local, national and international levels. Key stakeholders are clearly identified: public in general, academia, secondary education students, industry, decision makers, media, and patient organisations.

Ongoing

ERIBA Science Hall

ERIBA Science Hall is located at the ground floor of the building. It's a permanent exhibition about the research work carried out by the various laboratories of the Institute. It assembles a collection of interactive exhibits mainly addressed to students in the highest levels of secondary education in order to make them more familiar with and interested about scientific research

The Science Hall currently hosts the following exhibits:
- The Ageing Machine
- Cell Zoomer (to be discontinued in 2017)
- eMotion (to be discontinued in 2017) (*)
- Fountain of Youth
- The Living Cell (to be discontinued in 2017)
- Meet ERIBA Researchers
- ERIBA Animations
- Lifelines (**)

In 2017, three new exhibits will be added to the current portfolio:
- The Evolution of Data (an artistic movie about the evolution of data over the past 400 years, made in honour of the 400 year anniversary of the University of Groningen)
- ERIBA in images
- ERIBA supermodels

A dedicated website has been created to offer users a fascinating look in the world of biology and the science behind ageing.
(*) This exhibit was developed by the Dept. of Movement Science of UMCG
(**) This exhibit was developed by Mark Winkel

eribasciencehall.nl

Staff Members Involved All PIs, Outreach Officers (A. Steen collaborated with the development of the ERIBA Supermodels exhibit)
Audience General Public, Secondary Education Schools
N. of Participants/Visitors ~3.000 Visitors (2013-2016)

2014

ERIBA Corporate Video

This video was commissioned to present and introduce ERIBA to a lay audience. It has been often used in public talks/lectures.

eriba.umcg.nl/future-events/media-kit

Staff Members Involved Chang, de Haan, Lansdorp, Veenhoff, Outreach Officers, video and documentary experts
Audience General Public, Prospective Students, Scientists, Media, Stakeholders
N. of online visitors 306

Ongoing

PIs Profile Videos

Each PI has been given the opportunity to share his/her research expertise and future directions in short videos available at ERIBA website and on Vimeo channel.
Three more videos will be produced in 2017 for the recently recruited PIs (Demaria, Paeschke, Paridaen).
All videos are subtitled in Dutch.

eriba.umcg.nl/people/eugene-berezikov
eriba.umcg.nl/people/cor-calkhoven
eriba.umcg.nl/people/michael-chang
eriba.umcg.nl/people/maria-colome-tatche
eriba.umcg.nl/people/floris-foijer
eriba.umcg.nl/people/victor-guryev
eriba.umcg.nl/people/gerald-de-haan
eriba.umcg.nl/people/peter-lansdorp
eriba.umcg.nl/people/ellen-nollen
eriba.umcg.nl/people/liesbeth-veenhoff
vimeo.com/111731693

Staff Members Involved All PIs, Outreach Officers, video and documentary experts
Audience General Public Prospective Students, Scientists, Media
N. of online visitors 18.459

Released

Explanatory animations (explanimations)

Several PIs have developed, together with graphic designers, Animations to explain core research topics related with the work carried out in the labs. These animations, conceived in beautiful graphic techniques are an easy-to-follow manner to understand a complex problem in a short storyline. All animations are narrated both in Dutch and Engish.

Stem Cells, Fountain of Youth
vimeo.com/182878134

Staff Members Involved de Haan, Reijnen
Audience General Public, Prospective Students, Scientists, Media
N. of online visitors 186

Cellular Ageing
vimeo.com/111736259

Staff Members Involved Veenhoff, Rico
Audience General Public, Prospective Students, Scientists, Media
N. of online visitors 2.416

A worm to understand brain diseases of ageing
vimeo.com/125662586

Staff Members Involved Mata Cabana, Nollen, Rico, Reijnen
Audience General Public, Prospective Students, Scientists, Media
N. of online visitors 1.716

Aneuploidy: cell division slipped out of gear
vimeo.com/192920592

Staff Members Involved Foijer, Reijnen
Audience General Public, Prospective Students, Scientists, Media
Released in December 2016

Ongoing

Marriage Website

Marriage (Marie Curie Ageing Network) is a large scale EU funded project (€M4), aiming at training and teaching the next generation of scientists in the emerging field of ageing. The Network consists of 10 full and two associated partners, representing seven Member states and Switzerland and Canada, and includes four commercial enterprises.

ageingnetwork.eu

Staff Members Involved de Haan and Rodrigues
Audience General Public,Prospective Students, Scientists, Media
N. of Participants/Visitors ~20.000 visitors

Ongoing

PloidyNet Website

PloidyNet is a Marie Curie Initial Training Network (ITN) financed by the EU FP7 in the context of People-Marie Curie Actions, focussing on aneuploidy.The scientific aim of this network is to determine and compare the molecular consequences of different levels of aneuploidy, both in vivo and in vitro. Nine Early Stage Career and two Experienced researchers in the aneuploidy field have been selected world-wide and the network comprises 12 partners originating from five countries, and includes three commercial enterprises. Trainees will thus become experts in the field of aneuploidy while rapidly building up a scientific network for themselves, putting them in an excellent position to become future leaders in this field.

aneuploidy.nl

Staff Members Involved Foijer, Rodrigues, Reijnen
Audience General Public,Prospective Students, Scientists, Media
N. of Visitors ~100.000 visitors

2014

PloidyNet Video

The PloidyNet consortium has produced a video which assembles testimonies of the fellows involved in the project, aiming at sharing the importance of these kind of international training programmes for the career of young researchers in the context of International cooperation and education at the highest level.

vimeo.com/130432461

Staff Members Involved Foijer and Rodrigues, PloidyNet Fellows
Audience Prospective doctoral students

2015

Molecular Biology of Ageing Meeting

The meeting was organised for the first time in Groningen as an opportunity for scientists working in relevant areas related with ageing to meet on a regular basis and therefore do speak with one voice. The organisers brought together leading scientists interested in the biology of ageing who presented their work to a wide audience of young and established researchers and participated in open discussions on multiple aspects of ageing. The Meeting was co-organised by Jan Hoeijmakers, Erasmus MC Rotterdam. A second edition will be organised in 2017 (8-11 October)

bioageing.nl

Staff Members Involved Lansdorp, de Haan, Rico
Audience Scientists, Students, Commercial and Industrial Partners
N. of Participants 263 delegates

Ongoing

Visits of National and International Delegations

ERIBA has hosted ~80 delegations since its Official opening

Staff Members Involved All PIs, Managing Director, Outreach Officers
Audience Academia, Industry, Decision-Makers, Diplomatic Delegations
N. of Visitors ~80 delegations

Lectures and other activities for schools

2013

Short lectures about ERIBA research for the Junior Honours College

Staff Members Involved Van Zanten/several Postdoctoral fellows
Audience High school students

2014

Talk at 'Europese Kijkdagen' including laboratory tour

Staff Members Involved Foijer
Audience General Public
N. of Participants/Visitors ~ 20 people

2014

Outreach Event

Staff Members Involved Foijer
Audience Highschool Students

2014

Talk at TEDx event at Dublin, Ireland, on chromosomal instability and ageing, as an outreach about basic science

Staff Members Involved Foijer
Audience Local audience
N. of Participants/Visitors ~ 100 people. (Internet broadcasted)

2014

Talk at 'Natuurwetenschappelijk Genootschap Assen, about ageing and genomic instability

Staff Members Involved Foijer
Audience Educated laymen
N. of Participants/Visitors ~60 people

2014

Invited lecture/class at high school in Leek about mitosis . The event was connected to a contest to make best mitosis movie on YouTube

Staff Members Involved Foijer
N. of Participants/Visitors ~100 students

Ongoing since 2014

Host of several high school students for their biology research projects (typically 2-3 visits in which the students perform simple laboratory experiments and write a report). The objective is to have high school students experiencing life in the laboratory as well as contributing to their obligatory biology high school projects.

Staff Members Involved Foijer and Laboratory Members
Audience Highschool students
N. of Participants/Visitors 4 groups

Ongoing since 2014
Hosted several high school students for their biology research projects (typically 2-3 visits in which the students perform simple laboratory experiments and write a report. The objective is to have high school students experiencing life in the laboratory as well as contributing to their obligatory biology high school projects
Staff Members Involved Veenhoff and Laboratory Members
Audience Highschool students
N. of Participants/Visitors 3 groups (2-4 per group)

Ongoing since 2014
Hosted several high school students for their biology research projects (typically 2-3 visits in which the students perform simple laboratory experiments and write a report. The objective is to have high school students experiencing life in the laboratory as well as contributing to their obligatory biology high school projects
Staff Members Involved de Haan and Laboratory Members
Audience Highschool students

2014
Invited lecture/class at primary school about bacteria. Objective: stimulate interest in biology with primary school students
Staff Members Involved Veenhoff
Audience Primary school students

2014
Lecture on ageing addressed Academie Minerva students who were participating in an art-project with exhibition on the theme 'BeeldenvanBuiten'. The art students were researching the theme of ageing, using photography as a method of expression. The PI gave feedback on the projects
Staff Members Involved Veenhoff
Audience University students

2015
Lecture High School Teacher Day organised by ScienceLinx, University of Groningen: "Stamcellen en veroudering".
Staff Members Involved de Haan
Audience General Public
N. of Participants/Visitors 50 participants

2015
Tour and introduction ERIBA for Students Vitaliteitsmanagement & Toerisme; HZ University of Applied Sciences Vlissingen
Staff Members Involved Middelberg
Audience Students

2015
Visit Science Hall and Introduction to ERIBA for UMCG Next Trainees
Staff Members Involved Reijnen
Audience UMCG trainees, non-experts
N. of Participants/Visitors 25 participants

2016
Visit Science Hall and Introduction to ERIBA for keuzecollege Biomedische Technologie (4 vwo)
Staff Members Involved Reijnen
Audience High school students
N. of Participants/Visitors 40 participants

2016
Visit Science Hall and Introduction to ERIBA for foreign first year students of the University of Groningen for the event "Experience Groningen"
Staff Members Involved Reijnen
Audience University Students
N. of Participants/Visitors 60 participants

2016
Lecture at the Northerns Alliance
Staff Members Involved Veenhoff
Audience Interested non-experts

2016
Lecture at the Commerciele Club Groningen
Staff Members Involved Veenhoff
Audience Interested non-experts

2016
Weekend van de Wetenschap: "Onsterfelijk door stamcellen? ERIBA-Groningen, The Netherlands
Staff Members Involved de Haan
Audience General Public
N. of Participants/Visitors 40 participants

2016
Kenniscafé Emmen. Stamcellen; verleden, heden en toekomst, organised by Stenden Hogeschool Emmen, The Netherlands
kenniscafe-emmen.nl/Evenementen/Stamceltechnologie.html
Staff Members Involved de Haan
Audience Lay audience
N. of Participants/Visitors 160 participants

2016
TEDx Career Talk Mebiose (Student Association) Utrecht, The Netherlands
Staff Members Involved de Haan
Audience Life Science Students
N. of Participants/Visitors 100 participants

2016
Selling your science; How to write a successful paper and grant application. 45th Annual meeting of the International Society for Experimental Hematology, San Diego, US
Staff Members Involved de Haan
Audience General Public
N. of Participants/Visitors 100 young scientists

Media and Events

2012
GA Groningen
Staff Members Involved Teuling
Audience General Public

2013
Opening ERIBA ART
Staff Members Involved Teuling
Audience General Public

2013
Europa Kijkdagen
Staff Members Involved Teuling
Audience General Public

2013
ERIBA at "The night of Art and Science"
Staff Members Involved Teuling
Audience General Public

2013
National News Performance (NOS Journal 3/11/2013) on the occasion of opening of ERIBA
Staff Members Involved de Haan/Nollen
Audience General Public

2013
Guest in Talkshow at Omrop Fryslân at the occasion of the opening of ERIBA
Staff Members Involved de Haan
Audience General Public

2013
ERIBA at "Noorderzon"
Staff Members Involved de Haan
Audience General Public
N. of Participants/Visitors 100 young scientists

2013
Radio 1 journaal: interview "de dans naar de dood" opening of ERIBA
weblogs.nos.nl/radio1journaal/2013/11/07/de-dans-naar-de-dood
Staff Members Involved Teuling
Audience General Public

–
"Gezond ouder worden". Film porduced for UMCG KidsInZicht
www.umcg.nl/NL/Zorg/Kinderen/KidsInZicht/Paginas/Oud.aspx
Staff Members Involved de Haan
Audience General Public/children

2014
"Een heel lang en gezond leven". Interview with Eefje Oomen, Algemeen Dagblad
Staff Members Involved de Haan
Audience General Public

2014
Appearance in KRO's Brandpunt
Staff Members Involved de Haan
Audience General Public

2014
Interview for Libelle
Audience General Public

2014
Interview OOG Radio, Groningen
Staff Members Involved de Haan
Audience General Public

2014
Interview EditieNL, RTL4, Dutch National TV.
Staff Members Involved de Haan
Audience General Public

2014
Volkskrant: article "Matig eten verlengt leven"
www.volkskrant.nl/dossier-archief/matig-eten-verlengt-leven~a3626576/
Staff Members Involved Calkhoven
Audience General Public

2014
Science Café Groningen organized by Studium Generale, under the title "Alzheimer: causes and prevention"
Staff Members Involved: Nollen
Audience General Public

2015
Interview RTLZ, Dutch National TV
Staff Members Involved de Haan
Audience General Public

2015
"Details van het ouder worden". Interview for the Riepe, Street journal for Northern Netherlands, issue 209
Staff Members Involved de Haan
Audience General Public

2015
Let's GRO. Science and Culture Festival Groningen. Seminar "Biology of Ageing" (De biologie van veroudering)
Staff Members Involved de Haan
Audience General Public

2015
Volkskrant: article "Groningse muis eet alles en blijft toch gezond"
volkskrant.nl/wetenschap/groningse-muis-eet-alles-en-blijft-toch-gezond~a4095100
Staff Members Involved Calkhoven
Audience General Public

2016
Interview BNR Nieuws Radio: Xenotransplantie
Staff Members Involved de Haan
Audience General Public

2016
Sir Edmund - Volkskrant magazine: Interview for article "Stop de tijd!" – Langer leven
volkskrant.nl/wetenschap/kunnen-wij-het-ouder-worden-vertragen~a4382330
Staff Members Involved Calkhoven
Audience General Public

2016
Interview for City of Talent – Marketing Groningen
Staff Members Involved Calkhoven
Audience General Public

2016
Presentation at ERIBA for the delegation from the City of Bremen with the Mayor of Bremen
Staff Members Involved Calkhoven and Grove
Audience Decision-makers

2016
Inauguration ERIBA-ScreeningPort strategic alliance. Part of the Groningen delegation with the Mayor of Groningen City and Commissioner of the King of Groningen Province (Hamburg, Germany)
Staff Members Involved Calkhoven
Audience Academia, Industry, decision-makers

2016
Plusklas project "The year 2046"
Staff Members Involved Reijnen
Audience General Public
N. of Participants/Visitors 20

2016
Zpannend Zernike/Weekend van de Wetenschap
Staff Members Involved Reijnen, Steen
Audience General Public
N. of Participants/Visitors 900

2016
Children's Book Week "Forever Young"
Staff Members Involved Reijnen
Audience Primary school children
N. of Participants/Visitors 26

2016
Klokhuis episode "Groter groeien", NPO 3 channel
hetklokhuis.nl/tv-uitzending/3369/Groter%20groeien
Staff Members Involved Nollen, Koopman, Reijnen
Audience Regular TV audience (children < 12)

2016
Science Café Nijmegen on "Genome stability and ageing"
Staff Members Involved Lansdorp
Audience General Public

Publications

2012
Biology of Ageing. Gerald de Haan. Geron, Magazine on Ageing, Nr. 4, blz. 7-10.
Staff Members Involved de Haan
Audience General Public

2013
Biology of Ageing. G. de Haan: in Bijblijven; Magazine about general medical practice, 67-70.
Staff Members Involved de Haan
Audience Family doctors

2016
JAN Groot, K. Klauke, G. Huls, G de Haan: "Leeftijdsgerelateerde klonale hematopoiese ten gevolge van mutaties in genen betrokken bij DNA-methylatie en histonmodificaties." Dutch Magazine on Hematology.
Staff Members Involved de Haan et al
Audience Dutch hematologists

9. Facts and Figures

Staff in numbers

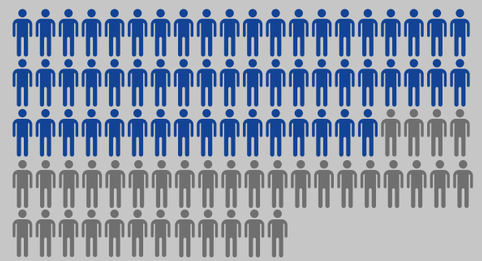
EMPLOYEES

2016

92

2013 · **81**
2014 · **89**
2015 · **89**

STAFF UNDER 40 (%)

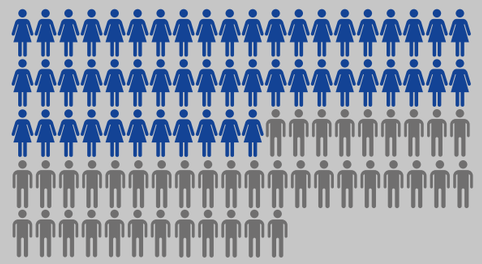


2016

61%

2013 · **69%**
2014 · **63%**
2015 · **63%**

FEMALE EMPLOYEES

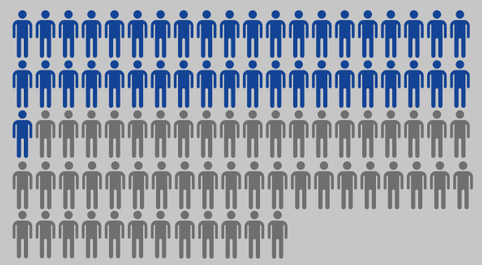


2016

55%

2013 · **60%**
2014 · **56%**
2015 · **56%**

INTERNATIONALS



2016

45%

2013 · **47%**
2014 · **48%**
2015 · **47%**

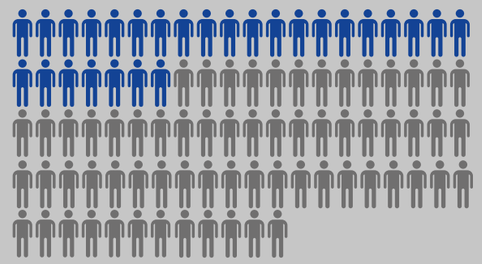
NUMBER OF NATIONALITIES

2016

22

2013 · **18**
2014 · **17**
2015 · **17**

DOCTORAL STUDENTS

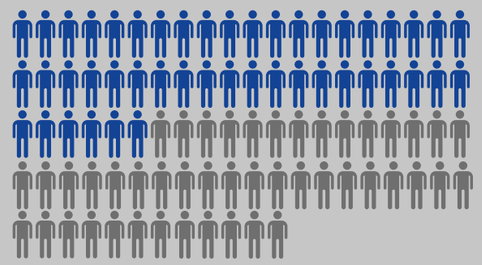


2016

27

2013 · **22**
2014 · **22**
2015 · **26**

INTERNS (*)



2016

26

2013 · **17**
2014 · **41**
2015 · **41**

(*) students who made internships in various labs

List of Staff Members (2011-2016) and former Students/Employees

	TEAM	PERIOD	CURRENT POSITION (Former Students and Staff)
PRINCIPAL INVESTIGATORS			
Berezikov, Eugene	BEREZIKOV	2012-present	----
Calkhoven, Cor	CALKHOVEN	2013-present	----
Chang, Michael	CHANG	2011-present	----
Colomé-Tatché, Maria	COLOMÉ-TATCHÉ	2013-present	----
Demaria, Marco	DEMARIA	2015-present	----
Foijer, Floris	FOIJER	2011-present	----
Guryev, Victor	GURYEV	2012-present	----
Haan, Gerald de	DE HAAN	2011-present	----
Lansdorp, Peter	LANSDORP	2011-present	----
Nollen, Ellen	NOLLEN	2014-present	----
Paeschke, Katrin	PAESCHKE	2016-present	----
Paridaen, Judith	PARIDAEN	2016-present	----
Riedel, Christian	RIEDEL	2013-2015	PI at the Dept. of Medicine, Karolinska Institute, Sweden
Veenhoff, Liesbeth	VEENHOFF	2012-present	----
RESEARCH ASSOCIATES AND POSTDOCTORAL FELLOWS			
Belderbos, Mirjam	DE HAAN	2013-present	----
Bevova, Marianna	LANSDORP	2013-present	----
Bystrykh, Lenja	DE HAAN	2011-present	----
Cabrera, Margarita	CHANG	2014-2015	Ramon y Cajal Fellow Oxidative Stress and Cell Cycle Research Group Universitat Pompeu Fabra (Barcelona, Spain)
Garcia Linares, Carles	LANSDORP	2013-2015	----
Garcia Martinez, Jorge	FOIJER	2014-2015	----

	TEAM	PERIOD	CURRENT POSITION (Former Students and Staff)
Hartleben, Götz	CALKHOVEN	2013-2015	Postdoctoral fellow, Institute for Diabetes and Cancer, Helmholtz Center Münich, Germany
Heyink, Anne Margriet	LANSDORP	2016-present	----
Hoffmann, Roland	LANSDORP	2013-2014	----
Juranek, Stefan	FOIJER	2016-present	----
Klauke, Karin	DE HAAN	2013-2016	Medical Advisor on Hematologie, Novartis, The Netherlands
Lui, Weilin	FOIJER	2016-present	----
Mata Cabana, Alejandro	NOLLEN	2012-present	----
Merzouk, Sarra	LANSDORP	2014-2016	Postdoctoral fellow, Erasmus MC, Rotterdam
Mouton, Stijn	BEREZIKOV	2013-present	----
Müller, Christine	CALKHOVEN	2013-present	----
Nawijn, Martijn	DE HAAN	2012-2013	Postdoctoral fellow Medical Biology department UMCG
Novarina, Daniele	CHANG	2014-present	----
Olivieri,Daniel	BEREZIKOV	2013-2014	Postdoctoral fellow, Friedrich Miescher Institute for Biomedical Research, Switzerland
Ovchinnikova, Ekaterina	BEREZIKOV	2013- present	----
Pandey, Satya	PAESCHKE	2016- present	----
Simanov, Dan	BEREZIKOV	2014-2015	Postdoctoral fellow, Hubrecht Institute, The Netherlands
Spierings, Diana	LANSDORP	2011-present	----
Steen, Anton	VEENHOFF	2012-present	----
Uringa, Evert-Jan	LANSDORP	2012-2015	Application Scientists, Taconic Biosciences GmbH, Germany
Verovskaya, Evgenia	DE HAAN	2014-2015	Postdoctoral fellow, University of California, US
Warmerdam, Daniël	FOIJER	2016-present	----
Weissert, Philipp	BEREZIKOV	2013-present	----
DOCTORAL STUDENTS			
Ackermann, Tobias	CALKHOVEN	2013-present	
Bakker,Bjorn	FOIJER	2013-present	----
Bos, Hilda van den	LANSDORP	2013-present	----
Claussin, Clemence	CHANG	2012-present	----
Dinitzen, Alexander	DE HAAN	2016-present	----
Flohr Svendsen, Arthur	DE HAAN	2016-present	----

	TEAM	PERIOD	CURRENT POSITION (Former Students and Staff)
Goot, Annemieke van der	NOLLEN	2012-2013	Postdoctoral fellow, Stanford University, US
Jilderda, Laura	FOIJER	2016-present	----
Janssen, George	VEENHOFF	2013-2016	Postdoctoral fellow, Karolinska Institute, Sweden
Jong, Tristan de	GURYEV	2014-present	----
Jung,Johannes	DE HAAN	2013-present	----
Koopman, Mandy	NOLLEN	2015-present	----
Kralt,Annemarie	VEENHOFF	2013-2016	Postdoctoral fellow, Institute of Biochemistry, ETH, Switzerland
Laba, Justyna	VEENHOFF	2012-2014	Senior Scientific Information Specialist at Elsevier, The Netherlands
Lawton-Grudniewska, Magda	BEREZIKOV	2012present	----
Lazare, Seka	DE HAAN	2013-present	----
Lin, Xin-Xuan	RIEDEL	2013-2015	Doctoral Student, Karolinska Institute, Sweden
Luinenburg, Daniëlle	DE HAAN	2016-present	----
Michels, Helen	NOLLEN	2012-present	----
Mourik, Paula van	CHANG	2013-present	----
Popken, Petra	VEENHOFF	2012-2014	Data Manager, PRA Health Sciences, The Netherlands
Porubsk, David	LANSDORP	2012-present	----
Pras, Anita	NOLLEN	2013-present	----
Radulovic, Vi nja	DE HAAN	2011-2016	Postdoctoral fellow, Lund University, Sweden
Rempel, Irina	VEENHOFF	2014-present	----
Russo Krauss, Sara	DE HAAN	2012-2016	Science Writer, Cochrane Society, University of Copenhagen, Denmark
Schukken, Klaske	FOIJER	2014-present	----
Schwindt, Eike	PAESCHKE	2016-present	----
Sen, Ilke	RIEDEL	2013-present	Doctoral Student, Karolinska Intitute, Sweden/ERIBA, UMCG, The Netherlands
Simon ,Judith	FOIJER	2013-present	----
Sin, Olga	NOLLEN	2012-2016	Postdoctoral fellow, Max Planck Institute for Molecular Biomedicine Muenster, Germany
Sterken, Britt	CALKHOVEN	2016-present	----
Stinus Ruiz de Gauna, Sonia	CHANG	2013-present	----
Stroo-van Riek, Esther	NOLLEN	2012-present	----
Taudt, Aaron	COLOMÉ-TATCHÉ	2013-present	----
Ustyantsev, Kirill	BEREZIKOV	2016-present	----
Vliet, Thijmen van	DEMARIA	2016-present	----
Wang, Boshi	DEMARIA	2016-present	----
Wietmarschen, Niek van	LANSDORP	2011-present	----
Wójtowicz,Edyta	DE HAAN	2011-2016	Postdoctoral fellow, Karolinska Institute, Sweden/ERIBA, UMCG, The Netherlands
Wudarski,Jakub	BEREZIKOV	2012-present	----
Zaini,Mohamad	CALKHOVEN	2013-present	----
Zhu,Yinan	FOIJER	2013-2014	Medical Science Liaison, AstraZeneca Pharmaceuticals, China

TECHNICIANS AND BIOINFORMATICIANS

Bakker, Petra	FOIJER	2012-present	----
Beltman, Frank	BEREZIKOV	2014-present	----
Brandenburg, Simone	DEMARIA	2013-present	----
Broekhuis, Mathilde	FOIJER	2011-present	----
Chan, Yin Fai	Management	2012-present	----
Dethmers-Ausema, Bertien	DE HAAN	2011-present	----
Glazenburg, Lisa	BEREZIKOV	2012-present	----
Grelling, Margriet	BEREZIKOV	2015-present	----
Halsema, Nancy	LANSDORP	2012-present	----
Hoekstra-Wakker, Karina	LANSDORP	2014-present	----
Hogewerf,Wytse	NOLLEN	2011-present	----
Huizinga, Eslie	FOIJER	2016-present	----
Jacobs, Sabrina	DE HAAN	2016-present	----
Jong, Jannie de	CHANG	2012-present	----
Kazemier, Inge	LANSDORP	2013-present	----
Kortman, Gertrud	CALKHOVEN	2014-present	----
Koster, Taco	DE HAAN	2013-2015	Brains Online, The Netherlands
Paruchuru,Sai	DE HAAN	2015-present	----
Radstaak, Marloes	DE HAAN	2014-2016	Applications Specialist, DOXX BV, The Netherlands
Ritsema, Martha	MCCA	2011-present	----
Seinstra, Renée	NOLLEN	2011-present	----
Staal, Jorn	LANSDORP	2016-present	----
Weersing, Ellen	DE HAAN	2011-present	----
Zwart, Erik	DE HAAN	2011-present	----

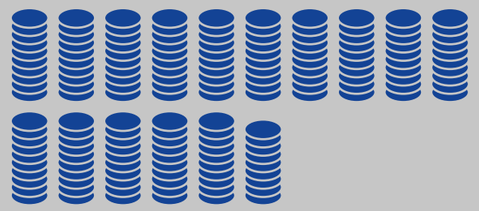
MANAGEMENT

Grove, Craig	TTO/Business Developer	2013-present	----

	TEAM	PERIOD	CURRENT POSITION (Former Students and Staff)
Heidekamp, Henk	Managing Director	2011-present	----
Hoks, Sylvia	Secretary	2013-present	----
Kool, Nina	Secretary	2015-present	----
Kuipers-van der Laan, Maria	Secretary	2013-2015	----
Martens, Klaas	Financial Officer	2014-present	----
Middelberg, Jutta	Outreach Officer	2014-2015	Manager Marketing & Communication, Energy Academy Europe, The Netherlands
Moes, Harry	Staff Advisor	2014-present	----
Reijnen, Femke	Outreach Officer	2015-present	----
Rico, Helena	Staff Advisor	2011-present	----
Rodrigues, Catarina	Research Officer	2013-present	----
Rozema, Arnoud	Staff Advisor	2015-present	----
Teuling, Eva	Outreach Officer	2011-2013	Project coordinator, Science LinX, University of Groningen
Vos-Hassing, Annet	Secretary	2011-present	----
Zanten-Timmer, Ineke van	Outreach Officer	2013-2014	Opniehof, The Netherlands

Funding

EXTERNAL FUNDING (GRANTS)



2016

€ 4,5M

2011/2012 · **€ 19,2M**
2013 · **€ 1,41M**
2014 · **€ 0,64M**
2015 · **€ 1,83M**

Publications

NUMBER OF SCIENTIFIC PUBLICATIONS IN 2016

2016

40

2011 · **12**
2012 · **22**
2013 · **37**
2014 · **34**
2015 · **39**

PUBLICATIONS PER RESEARCH GROUP (2012-2016)

Laboratory of Stem Cell Regulation and Mechanisms of Regeneration
Group Leader: Eugene Berezikov
(in ERIBA since April 2014)

1. **Grudniewska M**, **Mouton S**, **Simanov D**, **Beltman F**, **Grelling M**, de Mulder K, Arindrarto W, **Weissert PM**, van der Elst S, **Berezikov E**. (2016). Transcriptional signatures of somatic neoblasts and germline cells in *Macrostomum lignano*. eLife 2016;5:e20607.

2. Isik M, Blackwell TK, **Berezikov E**. MicroRNA mir-34 provides robustness to environmental stress response via the DAF-16 network in *C. elegans*. Sci Rep 2016, 6:36766. doi: 10.1038/srep36766

3. Dueck A, Evers M, Henz SR, Unger K, Eichner N, Merkl R, **Berezikov E**, Engelmann JC, Weigel D, Wenzl S, Meister G. Gene silencing pathways found in the green alga Volvox carteri reveal insights into evolution and origins of small RNA systems in plants. BMC Genomics. 2016 Nov 2;17(1):853.

4. Vegter EL, Schmitter D, Hagemeijer Y**, Ovchinnikova ES**, van der Harst P, Teerlink JR, O'Connor CM, Metra M, Davison BA, Bloomfield D, Cotter G, Cleland JG, Givertz MM, Ponikowski P, van Veldhuisen DJ, van der Meer P, **Berezikov E**, Voors AA, Khan MA. Use of biomarkers to establish potential role and function of circulating microRNAs in acute heart failure. Int J Cardiol. 2016 Dec 1;224:231-239. doi: 10.1016/j.ijcard.2016.09.010.

5. Zadesenets KS, Vizoso DB, Schlatter A, Konopatskaia ID, **Berezikov E**, Schärer L, Rubtsov NB. Evidence for Karyotype Polymorphism in the Free-Living Flatworm, *Macrostomum lignano*, a Model Organism for Evolutionary and Developmental Biology. PLoS One. 2016 Oct 18;11(10):e0164915. doi: 10.1371/journal.pone.0164915.

6. Rodrigues M, Ostermann T, Kremeser L, Lindner H, Beisel C, **Berezikov E**, Hobmayer B, Ladurner P. Profiling of adhesive-related genes in the freshwater cnidarian Hydra magnipapillata by transcriptomics and proteomics. Biofouling. 2016 Oct;32(9):1115-1129.

7. Wu CC, Kruse F, Vasudevarao MD, Junker JP, Zebrowski DC, Fischer K, Noël ES, Grün D, **Berezikov E**, Engel FB, van Oudenaarden A, Weidinger G, Bakkers J. Spatially Resolved Genome-wide Transcriptional Profiling Identifies BMP Signaling as Essential Regulator of Zebrafish Cardiomyocyte Regeneration. Dev Cell. 2016

Jan 11;36(1):36-49. doi: 10.1016/j.devcel.2015.12.010. Epub 2015 Dec 31.

8. Bruno N, ter Maaten JM, **Ovchinnikova ES**, Vegter EL, Valente MA, van der Meer P, de Boer RA, van der Harst P, Schmitter D, Metra M, O'Connor CM, Ponikowski P, Teerlink JR, Cotter G, Davison B, Cleland JG, Givertz MM, Bloomfield DM, Dittrich HC, Pinto YM, van Veldhuisen DJ, Hillege HL, **Berezikov E**, Voors AA. MicroRNAs relate to early worsening of renal function in patients with acute heart failure. Int J Cardiol. 2016 Jan 15;203:564-9. doi: 10.1016/j.ijcard.2015.10.217. Epub 2015 Nov 11.

9. Chereji RV, Kan TW, **Grudniewska MK**, Romashchenko AV, **Berezikov E**, Zhimulev IF, **Guryev V,** Morozov AV, Moshkin YM. Genome-wide profiling of nucleosome sensitivity and chromatin accessibility in Drosophila melanogaster. Nucleic Acids Res. 2016 Feb 18;44(3):1036-51. doi: 10.1093/nar/gkv978. Epub 2015 Oct 1.
*JP

10. **Ovchinnikova ES**, Schmitter D, Vegter EL, Ter Maaten JM, Valente MA, Liu LC, van der Harst P, Pinto YM, de Boer RA, Meyer S, Teerlink JR, O'Connor CM, Metra M, Davison BA, Bloomfield DM, Cotter G, Cleland JG, Mebazaa A, Laribi S, Givertz MM, Ponikowski P, van der Meer P, van Veldhuisen DJ, Voors AA, **Berezikov E.** Signature of circulating microRNAs in patients with acute heart failure. Eur J Heart Fail. 2016 Apr;18(4):414-23. doi: 10.1002/ejhf.332. Epub 2015 Sep 8.

11. Desvignes T, Batzel P, **Berezikov E**, Eilbeck K, Eppig JT, McAndrews MS, Singer A, Postlethwait JH. miRNA Nomenclature: A View Incorporating Genetic Origins, Biosynthetic Pathways, and Sequence Variants. Trends Genet. 2015 Nov;31(11):613-26. doi: 10.1016/j.tig.2015.09.002. Epub 2015 Oct 8.

12. Hoffmann RF, Moshkin YM, **Mouton S**, Grzeschik NA, Kalicharan RD, Kuipers J, Wolters AH, Nishida K, Romashchenko AV, Postberg J, Lipps H, **Berezikov E**, Sibon OC, Giepmans BN, **Lansdorp PM**[9]. Guanine quadruplex structures localize to heterochromatin. Nucleic Acids Res. 2015 Sep 17. pii: gkv900. [Epub ahead of print]
*JP

13. Ikeda K, Horie-Inoue K, Ueno T, Suzuki T, Sato W, Shigekawa T, Osaki A, Saeki T, **Berezikov** E, Mano H, Inoue S. miR-378a-3p modulates tamoxifen sensitivity in breast cancer MCF-7 cells through targeting GOLT1A. Sci Rep. 2015 Aug 10;5:13170. doi: 10.1038/srep13170.

14. Arbore R, Sekii K, Beisel C, Ladurner P**, Berezikov E**, Schärer L. Positional RNA-Seq identifies candidate genes for phenotypic engineering of sexual traits. Front Zool. 2015 Jul 3;12:14. doi: 10.1186/s12983-015-0106-0. eCollection 2015. PMID: 26146508 Free PMC Article. Eur J Heart Fail.

15. Junker JP, Noël ES, **Guryev V**, Peterson KA, Shah G, Huisken J, McMahon AP, **Berezikov E,** Bakkers J, van Oudenaarden A. Genome-wide RNA Tomography in the Zebrafish Embryo. Cell. 2014 Oct 23;159(3):662-75. doi: 10.1016/j.cell.2014.09.038.
*JP

16. Babae N, Bourajjaj M, Liu Y, Van Beijnum JR, Cerisoli F, Scaria PV, Verheul M, Van Berkel MP, Pieters EH, Van Haastert RJ, Yousefi A, Mastrobattista E, Storm G, **Berezikov E**, Cuppen E, Woodle M, Schaapveld RQ, Prevost GP[5], Griffioen AW, Van Noort PI, Schiffelers RM. Systemic miRNA-7 delivery inhibits tumor angiogenesis and growth in murine xenograft glioblastoma. Oncotarget. 2014 Aug 30;5(16):6687-700.

17. Moroz LL, Kocot KM, Citarella MR, Dosung S, Norekian TP, Povolotskaya IS, Grigorenko AP, Dailey C, **Berezikov E**, Buckley KM, Ptitsyn A, Reshetov D, Mukherjee K, Moroz TP, Bobkova Y, Yu F, Kapitonov VV, Jurka J, Bobkov YV, Swore JJ, Girardo DO, Fodor A, Gusev F, Sanford R, Bruders R, Kittler E, Mills CE, Rast JP, Derelle R, Solovyev VV, Kondrashov FA, Swalla BJ, Sweedler JV, Rogaev EI, Halanych KM, Kohn AB. The ctenophore genome and the evolutionary origins of neural systems. Nature. 2014 Jun 5;510(7503):109-14. doi: 10.1038/nature13400. Epub 2014 May 21.

18. Lengerer B, Pjeta R, Wunderer J, Rodrigues M, Arbore R, Schärer L, **Berezikov E,** Hess MW, Pfaller K, Egger B, Obwegeser S, Salvenmoser W, Ladurner P. Biological adhesion of the flatworm *Macrostomum lignano* relies on a duo-gland system and is mediated by a cell type-specific intermediate filament protein. Front Zool. 2014 Feb 12;11(1):12. doi: 10.1186/1742-9994-11-12.

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Laboratory of Gene regulation in ageing and age-related diseases

Group Leader: Cor Calkhoven (in ERIBA since July 2013)

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Laboratory of Telomeres and Genome Integrity

Group Leader: Michael Chang
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Laboratory of Quantitative Epigenetics
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1. **Bakker, B., Taudt, A., Belderbos, M.E., Porubsky, D., Spierings, D.C., de Jong, T.V., Halsema, N., Kazemier, H.G.**, Hoekstra-Wakker, K., Bradley, A. et al. (2016) Single-cell sequencing reveals karyotype heterogeneity in murine and human malignancies. Genome Biol, 17, 115.

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Laboratory of Ageing Biology and Stem Cells
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Laboratory of Cellular Senescence and Age-related Pathologies

Group Leader: Marco Demaria
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1. Velarde MC, **Demaria M**. Targeting Senescent Cells: Possible Implications for Delaying Skin Ageing: A Mini-Review. Gerontology. 2016;62(5):513-8. doi: 10.1159/000444877. Epub 2016 Apr 1.

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Laboratory of Genomic Instability in Development and Disease

Group Leader: Floris Foijer (in ERIBA sinceAugust 2011)

1. **Bakker, B., Taudt, A., Belderbos, M.E., Porubsky, D., Spierings, D.C., de Jong, T.V., Halsema, N., Kazemier, H.G.**, Hoekstra-Wakker, K., Bradley, A. et al. (2016) Single-cell sequencing reveals karyotype heterogeneity in murine and human malignancies. Genome Biol, 17, 115.

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Laboratory of Genome Structure and Ageing

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1. **Porubsk D**, Sanders AD, **van Wietmarschen N**, Falconer E, Hills M, **Spierings DC, Bevova MR, Guryev V, Lansdorp PM**. Direct chromosome-length haplotyping by single-cell sequencing. Genome Res. 2016. 26:1565-1574.

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Laboratory of Nucleic Acids Structures and Repair

Group Leader: Katrin Paescke (in ERIBA since May 2016)

1. Philips JA, Chan A., **Paeschke K**, Zakian VA. (2015) The Pif1 helicase, a negative regulator of telomerase, acts preferentially at long telomeres. PLoS Genet.

2. Bochman ML, **Paeschke K**, Chan A, Zakian VA. (2014) Hrq1, a Homolog of Human RecQ4 Helicase, Acts Catalytically and Structurally to Promote Genome Integrity. Cell Rep.

3. **Paeschke K**, Bochman ML, Garcia PD, Cejka P, Friedman KL, Kowalczykowski SC, Zakian VA (2013). Pif1 family helicases suppress genome instability at G-quadruplex motifs. Nature. 497, 458–462 (23 May 2013) doi:10.1038/nature12149

4. Bochman ML, **Paeschke K**, Zakian VA (2012). DNA secondary structures: stability and function of G-quadruplex structures. Nature Genet. 13, 770-780 (November 2012) | doi:10.1038/nrg3296

5. Juranek S.A., **Paeschke K**. (2012). Cell Cycle Regulation of G-quadruplex DNA Structures at Telomeres. Curr Pharm Des.

Laboratory of Asymmetric Cell Division and Ageing

Group Leader: Judith Paridaen
(in ERIBA since January 2016)

1. Paridaen JT, Huttner WB, Wilsch-Bräuninger M. Analysis of primary cilia in the developing mouse brain. Methods Cell Biol. 2015;127:93-129. doi: 10.1016/bs.mcb.2014.12.012.

2. **Paridaen JTML** and Huttner WB. (2014). Neurogenesis during development of the vertebrate central nervous system. EMBO reports. 2014 Apr;15(4):351-64. doi: 10.1002/embr.201438447. Epub 2014 Mar 17.

3. **Paridaen JTML**, Wilsch-Bräuninger M, Huttner WB. (2013). Asymmetric inheritance of centrosome-associated primary cilium membrane directs ciliogenesis after cell division. Cell. 2013 Oct 10;155(2):333-44. doi: 10.1016/j.cell.2013.08.060.

4. Wilsch-Bräuninger M, Peters J, **Paridaen JTML**, Huttner WB. (2011). Basolateral rather than apical primary cilia on neuroepithelial cells committed to delamination. Development. 2012 Jan;139(1):95-105. doi: 10.1242/dev.069294. Epub 2011 Nov 17.

5. **Paridaen JTML**, Janson E, Utami KH, Pereboom TC, Essers PB, van Rooijen C, Zivkovic D, MacInnes AW. (2011). The nucleolar GTP-binding proteins Gnl2 and nucleostemin are required for retinal neurogenesis in developing zebrafish. Dev Biol. 2011 Jul 15;355(2):286-301. doi: 10.1016/j.ydbio.2011.04.028. Epub 2011 Apr 30.

Laboratory of Molecular Mechanisms in Lifespan Regulation

Group Leader: Christian Riedel (in ERIBA between January 2013 and September 2015)

1. Heimbucher T, Liu Z, Bossard C, McCloskey R, Carrano AC, **Riedel CG**, Tanasa B, Klammt C, Fonslow BR, Riera CE, Lillemeier BF, Kemphues K, Yates JR 3rd, O'Shea C, Hunter T, Dillin A. The Deubiquitylase MATH-33 Controls DAF-16 Stability and Function in Metabolism and Longevity. Cell Metab. 2015 Jul 7;22(1):151-63. doi: 10.1016/j.cmet.2015.06.002.

Laboratory of Cellular Biochemistry

Group Leader: Liesbeth Veenhoff (in ERIBA since June 2012)

1. **Janssens, GE**, **Veenhoff, LM.** The natural variation in lifespans of single yeast cells is related to variation in cell size, ribosomal protein, and division time. PLOS accepted nov 2016, PONE-D-16-15986

2. **Janssens, GE**, **Veenhoff, LM.** Evidence for the hallmarks of human ageing in replicatively ageing yeast. MICROBIAL CELL, Volume: 3, Issue: 7, Pages: 263-274, DOI: 10.15698/mic2016.07.510 Published: JUL 2016

3. **Janssens GE**, Meinema AC, González J, Wolters JC, Schmidt A, **Guryev V**, Bischoff R, Wit EC, **Veenhoff LM**, Heinemann M. Protein biogenesis machinery is a driver of replicative ageing in yeast. Elife. 2015 Dec 1;4. pii: e08527. doi: 10.7554/eLife.08527. PMID: 26422514 ***JP**

4. **Laba JK**, **Steen A**, **Popken P**, Chernova A, Poolman B, **Veenhoff** LM. Active Nuclear Import of Membrane Proteins Revisited. Cells. 2015 Oct 13;4(4):653-73. doi: 10.3390/cells4040653.

5. **Kralt A**, Jagalur NB, van den Boom V, Lokareddy RK, **Steen A**, Cingolani G, Fornerod M, **Veenhoff LM**. Conservation of inner nuclear membrane targeting sequences in mammalian Pom121 and yeast Heh2 membrane proteins. Mol Biol Cell. 2015 Jul 15. pii: mbc.E15-03-0184. [Epub ahead of print]

6. Lokareddy RK, **Hapsari RA**, van Rheenen M, Pumroy RA, Bhardwaj A, **Steen A**, **Veenhoff LM**, Cingolani G. Distinctive Properties of the Nuclear Localization Signals of Inner Nuclear Membrane Proteins Heh1 and Heh2. Structure. 2015 Jul 7;23(7):1305-16. doi: 10.1016/j.str.2015.04.017. Epub 2015 Jun 4.

7. **Popken P**, Ghavami A, Onck PR, Poolman B, **Veenhoff LM**. Size-dependent leak of soluble and membrane proteins through the yeast nuclear pore complex. Mol Biol Cell. 2015 Apr 1;26(7):1386-94. doi: 10.1091/mbc.E14-07-1175. Epub 2015 Jan 28.

8. **Kralt A**, Carretta M, Mari M, Reggiori F, **Steen A**, Poolman B, **Veenhoff LM**. Intrinsically disordered linker and plasma membrane-binding motif sort Ist2 and Ssy1 to junctions. Traffic. 2015 Feb;16(2):135-47. doi: 10.1111/tra.12243. Epub 2014 Dec 28.

9. Ghavami A, **Veenhoff LM**, van der Giessen E, Onck PR. Probing the disordered domain of the nuclear pore complex through coarse-grained molecular dynamics simulations. Biophys J. 2014 Sep 16;107(6):1393-402. doi: 10.1016/j.bpj.2014.07.060.

10. **Laba JK**, **Steen A**, **Veenhoff LM.** Traffic to the inner membrane of the nuclear envelope. Curr Opin Cell Biol. 2014 Jun;28:36-45. doi: 10.1016/j.ceb.2014.01.006. Epub 2014 Feb 13.

11. Meinema AC, Poolman B, **Veenhoff LM.** Quantitative analysis of membrane protein transport across the nuclear pore complex.Traffic. 2013 May;14(5):487-501. doi: 10.1111/tra.12048. Epub 2013 Feb 21.

12. Meinema AC, Poolman B, **Veenhoff LM**. The transport of integral membrane proteins across the nuclear pore complex. Nucleus. 2012 Jul 1;3(4):322-9. PMID:22614756 DOI: 10.4161/nucl.20439

***JP: Joint publications**

Awards

AWARDS AND PRIZES/DOCTORAL STUDENTS AND POSTDOCTORAL FELLOWS

Date	Awardee	Description
2016	Georges Janssens	Max Gruber Prize for the best peer reviewed publications of the University of Groningen in Biochemistry or Cell Biology (prize awarded biannually to the best publication produced by a doctoral student)
2016	Seka Lazare	Travel Award from the International Society for Experimental Hematology San Diego, US
2016	Mirjam Belderbos	Travel grant of the International Society for Hematology to attend their 2016 annual meeting
2016	Aaron Taudt	EMBO fellowship for my one-month stay, Cambridge, UK
2016	David Porubsky	EMBO short term Fellowship at the MAX-Planck- Institut für informatik Algorithms for Computational Genomics, Germany
2016	David Porubsky	ASHG 2016 Poster Walk Presentations , Vancouver, Canada
2016	Marianna Bevova	Teaching Excellence Fellowship by the University of Groningen, The Netherlands
2016	Maria Sarkis Azkanaz	Saxion Graduation Award for the best graduation project
2015	Seka Lazare	2nd prize for best poster at the Dutch Society for Stem Cell Research
2015	Esther Stroo	Travel grant from the Stiching Simonsfonds
2015	Esther Stroo	EMBO Short Term Fellowship to develop the project titled Visualizing the role of SERF in aggregation initiation in living cells
2015	Olga Sin	Simmons Fonds travel grant to attend the 20th International C. elegans Meeting, University of California, Los Angeles, US
2015	Bjorn Bakker	Best oral presentation at 3rd Annual Cancer Research Center Groningen Meeting
2015	Sonia Stinus	EMBO Short-Term Fellowship to learn experimental techniques in the laboratory of Dr. Brian Luke (IMB, Mainz), Germany
2015	Mandy Koopman	Avril McDonald Award for best female master student
2014	Karin Klauke	Max Gruber Prize for the best peer reviewed publications of the University of Groningen in Biochemistry or Cell Biology (prize awarded biannually to the best publication produced by a doctoral student)
2014	Annemieke van der Goot	Max Gruber Prize for the best peer reviewed publications of the University of Groningen in Biochemistry or Cell Biology (prize awarded biannually to the best publication produced by a doctoral student)
2014	Karin Klauke	Van Swinderen Prize 2014, awarded annually by the Koninklijk Natuurkundig Genootschap at Groningen to reward doctoral theses distinguished ‘cum laude’ obtained in the previous academic year
2014	David Porubsky	Best Poster Presentation at the 2nd Annual doctoral student meeting of the Cancer Research Centre Groningen, The Netherlands
2014	Evgenia Verovskaya	Rubicon Fellowship (Netherlands Organization for Scientific Research)
2013	Karin Klauke	New Investigator First Prize at the 42nd Annual Meeting of the international Society for Experimental Hematolgy, Vienna, Austria
2013	Edyta Woijowics	Else Kröner-Fresenius (EKF) Symposium on Adult Stem Cells in Ageing, Diseases and Cancer scheduled for May 31 – June 3, Erice Italy
2013	Johannes Jung	Best Abstract, Annual Meeting of the German Society of Hematology and Oncology, Germany
2013	Niek van Wietmarschen	Best poster, EMBO Conference, Cape Sounio, Greece
2013	Esther Stroo	Travel grant from the Stiching Simonsfonds

Invited Speakers

Date	External invited Speakers	Host	Title	Institute	Event
1/10/2013	Hinco Gierman	Floris Foijer	Whole genome sequencing of the world's oldest people	Stanford University, California, USA	Molecular Medicine Series
1/24/2013	Hein te Riele	Floris Foijer	Retinoblastoma: a genomic instability syndrome?	NKI, Amsterdam	Molecular Medicine Series
3/21/2013	Rocio Sotillo	Floris Foijer	Causes and Consequences of aneuploidy in Cancer	EMBL Monterotondo, Rome, Italy	Molecular Medicine Series
4/18/2013	Joachim Lingner	Michael Chang	Telomerase structure and its regulation at chromosome ends	École Polytechnique Fédérale de Lausanne, Switzerland	Molecular Medicine Series
4/25/2013	Rodney Rothstein	Michael Chang	Choreography of the DNA damage response: cell biological studies reveal increased chromosome dynamics during recombination	Columbia University, New York, USA	Molecular Medicine Series
5/16/2013	Shahragim Tajbakhsh	Gerald de Haan	Skeletal muscle stem cells in distinct cellular states	Dept. of Developmental & Stem Cell Biology, Pasteur Institute, Paris, France	Molecular Medicine Series
5/30/2013	Maarten van Lohuizen	Sophia Bruggeman	Screening for epigenetic targets and drug combinations in cancer	NKI, Amsterdam	Molecular Medicine Series
7/25/2013	John LaCava	Michael Chang	Complementary Tools Supporting Comprehensive Mapping of Protein Complexes via Affinity Capture / Mass Spectrometry"	Rockefeller University/New York University	Seminar at ERIBA
9/3/2013	Ester Falconer	Peter Lansdorp	Why one strand is better than two: sequencing only template strands expands the scope of single cell genomics	Terry Fox Laboratory (Lansdorp), Vancouver, Canada	Seminar at ERIBA
9/5/2013	Geraldine Aubert	Peter Lansdorp	How long are your telomeres: implications for cellular fitness and disease	Terry Fox Laboratory (Lansdorp), Vancouver, Canada	Seminar at ERIBA
9/6/2013	Anja Duursma	Floris Foijer	Molecular understanding of ATR activation: new insights into cancer and therapy	KWF fellow – Netherlands Cancer Institute; Rene Medema laboratory	Friday Afternoon Meeting
9/20/2013	Pradeep Kumar Singh	Ellen Nollen	Understanding the Mechanism of Protein Aggregation in Amyloid Diseases	Biosciences & Bioengineering Dept Indian Institute of Technology, Bombay	Seminar at ERIBA
9/26/2013	Ron Kopito	Ellen Nollen	Intra- and Inter- cellular effects of polyglutamine protein aggregation	Stanford University, Department of Biology	Seminar at ERIBA
10/4/2013	Ulrike Naumann	Peter Lansdorp	Single cell RNA sequencing for measuring DNA template strand specific gene expression in vivo	Terry Fox Laboratory	Seminar ERIBA
10/11/2013	Matthias Heinig	Maria Colomé-Tatché	HistoneHMM: differential analysis of histone modifications	Max Planck Institute for molecular genetics, Department Computational Molecular Biology, Berlin, Germany	Friday Afternoon Meeting
10/18/2013	Leonie Kamminga	Gerald de Haan	The Polycomb Group Gene ezh2 and the Maintenance of Cellular Identity	UMC St Radboud	Friday Afternoon Meeting
10/25/2013	Bill Schafer	Ellen Nollen	Sensory molecules and mechanisms in C. *elegans*	Cellular and molecular mechanisms of behaviour MRC Laboratory of Molecular Biology	Friday Afternoon Meeting
11/1/2013	Daphne Huibers	Liesbeth Veenhoff	Caloric restriction does not extend replicative lifespan in *Saccharomyces cerevisiae*	Matthias Heinema laboratory, University of Groningen, Molecular Systems Biology Group	Friday Afternoon Meeting
11/14/2013	Allan Bradley	Floris Foijer	Extreme genome engineering: humanizing the mouse immunoglobulin loci	Wellcome Trust Sanger Institute, Hinxton, Cambridge, UK	Molecular Medicine Series
11/15/2013	Ehud Cohen	Ellen Nollen	Two maladies, one mechanism – impaired cyclophilin activity underlies the development of distinct familial neurodegenerative disorders	Biochemistry and Molecular Biology, The Institute for Medical Research Israel-Canada (IMRIC), School of Medicine, The Hebrew University of Jerusalem, Israel	Friday Afternoon Meeting

Date	External invited Speakers	Host	Title	Institute	Event
11/28/2013	Geert Kops	Floris Foijer	Evolution and function of a regulatory network for error-free chromosome segregation	Dept. of Medical Oncology and Dept. Of Mol. Cancer Research, UMC Utrecht	Molecular Medicine Series
2/21/2014	Riekelt Houtkooper	Ellen Nollen	Mitochondrial function in ageing	AMC, Amsterdam	ERIBA seminar
2/28/2014	Peter Thorpe	Michael Chang	Re-engineering the cell, using protein relocation to dissect cell cycle control	MRC National Institute for Medical Research, London, UK	Friday Afternoon Meeting
3/6/2014	dr. Stefan Erkeland	Gerald de Haan	MicroRNAs miR-139-3p and miR-199a-3p Drive Bone Marrow Failure and Leukemic Transformation in Fanconi Anemia	Dept of Hematology, ErasmusMC, Rotterdam	ERIBA seminar
3/13/2014	Thorsten Hoppe	Christian Riedel	The role of protein degradation in proteostasis and stress response	Institute for Genetics and Cologne Excellence Cluster on Cellular Stress Responses in Ageing-Associated Diseases (CECAD), University of Cologne, Germany	Molecular Medicine Series
3/14/2014	Peter van Galen	Gerald de Haan	Molecular regulation of human hematopoietic stem cell self-renewal	Doctoral student Princess Margaret Cancer Centre, Toronto	Friday Afternoon Meeting
3/24/2014	Mark Hills	Peter Lansdorp	Of mice and men and Tasmanian devils; assembling reference genomes from single cells	BC Cancer Agency, Vancouver	ERIBA seminar
3/28/2014	Christopher E. Pearson, Doctoral student	Peter Lansdorp	DNA/RNA Repeat Instability: from Myotonic Dystrophy to Amyotrophic Lateral Sclerosis	Department of Genetics, Peter Gilgan Ctr for Research & Learning, Toronto	ERIBA seminar
4/10/2014	Bas van Steensel	Sophia Bruggeman	Genomics approaches to chromatin organization	NKI Amsterdam	Molecular Medicine Series
4/14/2014	Victor Kotelianski, M.D., Doctoral student., D.Sc.	Peter Lansdorp	In vivo RNAi and Functional Genomics	Visiting Fellow, Koch Institute (Dan Anderson's Laboratory)	ERIBA seminar

Date	External invited Speakers	Host	Title	Institute	Event
5/14/2014	Gilles Charvin	Liesbeth Veenhoff & Michael Chang	Single cell analysis of entry into replicative senescence in budding yeast	Institut de Génétique et de Biologie Moléculaire et Cellulaire, France	ERIBA seminar
6/5/2014	Julia von Mahltzahn, doctoral student	Cor Calkhoven	Non-canonical Wnt signaling in skeletal muscle	Leibniz Institute for Age Research – Fritz Lipmann Institute Jena, Germany	ERIBA seminar
6/18/2014	Kristina Schmidt, doctoral student	Peter Lansdorp	RecQ helicases - Guarding the genome against hyper-recombination	Department of Cell Biology, Microbiologyand Molecular Biology, University of South Florida	ERIBA seminar
6/18/2014	Danny M. Hatters, doctoral student	Ellen Nollen	Building windows into the cell to view protein folding, misfolding and aggregation	Department of Biochemistry and Molecular Biology, The University of Melbourne	ERIBA seminar
9/5/2014	Iris Jonkers	Peter Lansdorp	Detecting nascent transcription dynamics by GRO-seq in mouse ESCs	UMCG, Genetica	Friday Afternoon Meeting
9/25/2014	Jurgen Marteijn	Floris Foijer	Nucleotide Excision Repair and its interplay with Transcription	Erasmus MC, Rotterdam	Molecular Medicine Series
10/3/2014	Rob Coppes	Gerald de Haan	Salivary gland stem cells	UMCG, Departments of Radiation Oncology and Cell Biology, section Radiation & Stress Cell Biology	Friday Afternoon Meeting
10/9/2014	Zhao-Qi Wang	Cornelis F. Calkhoven	Epigenetic regulation in neural stem cell fate determination and neurodegeneration	Leibniz Institute for Age Research, Fritz Lipmann Institute, Jena, Germany	Molecular Medicine Series
10/24/2014	John LaCava	Michael Chang	Quantitative Differential Proteomic Analyses Dissect the Human LINE-1 Retrotransposon Ribonucleoprotein Physical Interactome	Rockefeller University/New York University	Friday afternoon ERIBA
10/30/2014	Axel Behrens	Cornelis F. Calkhoven	Pancreatic progenitor cells, fate reprogramming, and cancer	London Research Institute - Cancer Research, London, UK	Molecular Medicine Series

Date	External invited Speakers	Host	Title	Institute	Event
11/7/2014	Jan Philipp Junker	Eugene Berezikov	Genome-wide RNA tomography in the zebrafish embryo	Hubrecht Institute, Utrecht	Friday Afternoon Meeting
11/13/2014	Liza Pon	Liesbeth Veenhoff	Role for mitochondrial quality control during yeast cell division in ageing	Dept. of Pathology & Cell Biology and Institute of Human Nutrition, Columbia University, New York, USA	Molecular Medicine Series
11/14/2014	Ehud Cohen, doctoral student	Ellen Nollen	Two maladies, one mechanism – impaired cyclophilin activity underlies the development of distinct familial neurodegenerative disorders	Biochemistry and Molecular Biology, The Institute for Medical Research Israel-Canada (IMRIC), School of Medicine, The Hebrew University of Jerusalem, Israel	Friday Afternoon Meeting
11/20/2014	Michael Knop	Christian Riedel	Towards a dynamic visualisation of yeast proteome homeostasis	ZMBH, University of Heidelberg, Germany	Molecular Medicine Series
12/12/2014	Romana Schirhagl	Gerald de Haan	Free radical imaging using diamond magnetometry	UMCG, Department of Biomedical Engineering	Friday Afternoon Meeting
1/30/2015	Karl Duderstadt	Michael Chang	Single replication machines at work: the coordination of daughter strand synthesis	Antoine van Oijen Group, Single-Molecular Biophysics, Zernike Institute for Advanced Materials (ZIAM), Groningen, the Netherlands	Friday Afternoon Meeting
2/6/2015	Dario Valenzano	Cor Calkhoven	Genetics and genomics of lifespan in the short-lived African Turquoise Killifish	Max Planck Institute for Biology of Ageing, Cologne, Germany	Friday Afternoon Meeting
2/19/2015	Ralf Baumeister	Christian Riedel	Genetic and environmental factors contributing to stem cell tumors	University of Freiburg, Germany	Molecular Medicine Series
2/20/2015	Ody Sibon	Ellen Nollen	Coenzyme A: upside down and inside out	Dept. Celbiology, University Medical Centre Groningen, the Netherlands	Friday Afternoon Meeting
3/6/2015	Sake van Wageningen	Michael Chang	An evolutionarily conserved synthetic lethal interaction of RAS signalling	Netherlands Cancer Institute, Amsterdam, The Netherlands	Friday Afternoon Meeting

Date	External invited Speakers	Host	Title	Institute	Event
3/12/2015	Steven Szilvassy	Gerald de Haan	New tools for harnessing hematopoietic stem cell function to produce large numbers of primitive or mature cells	StemCell Technologies Vancouver, Canada	Molecular Medicine Series
4/2/2015	Michele De Luca	Gerald de Haan / Rob Coppes	Regenerative medicine by somatic stem cells; the paradigm of epithelialt stem cells	Centre for Regenerative Medicine "Stefano Ferrari"University of Modena and Reggio Emilia, Modena ,Italy	Molecular Medicine Series
4/10/2015	Brian Luke	Michael Chang	Nutritional signaling meets DNA damage: the unexpected link between TOR signaling, DNA damage checkpoints and lifespan	Institute of Molecular Biology, Mainz, Germany	Friday Afternoon Meeting
4/16/2015	Sebastien Smallwood	Maria Colomé-Tatché	DNA methylation dynamics during germ cell specification and early embryogenesis	Babraham Institute, Cambridge, UK	Molecular Medicine Series
4/30/2015	Johan Auwerx	Cor Calkhoven	Mitochondrial function and ageing	Ecole Plytechnique Federale de Lausanne, Suisse	Molecular Medicine Series
5/21/2015	Brad Johnson	Michael Chang	Mechanisms of senescence and pathology driven by telomere dysfunction	Dept. Of Pathology and Laboratory Medicine, University of Pennsylvania, Philadelphia, USA	Molecular Medicine Series
5/28/2015	Austin Smith	Gerald de Haan	The nature of pluripotent stem cells	Wellcome Trust/ MRCC Stem Cell Institute, University of Cambridge, UK	Molecular Medicine Series
6/5/2015	Fulvio Reggiori	Liesbeth Veenhoff / Michael Chang	Role of phosphatidylinositol-3-phosphate turnover in autophagosome completion	Dept. Celbiology, University Medical Centre Groningen, the Netherlands	Friday Afternoon Meeting
6/12/2015	Rodoniki Athanasi-adou	Michael Chang	Global tuning of gene expression through regulated RNA synthesis and degradation"	NYU, NY	Seminar ERIBA
7/20/2015	Ricardo Marchante	Ellen Nollen	Quantitative investigations into the molecular mechanisms of amyloid fibril fragmentation	Xue Laboratory, School of Biosciences, University of Kent, Canterbury, UK	Seminar ERIBA

Date	External invited Speakers	Host	Title	Institute	Event
10/8/2015	Rene Medema	Floris Foijer	Chromosome instability; driving genetic diversity; compromising cellular fitness	Netherlands Cancer Institute, Amsterdam, The Netherlands	Molecular Medicine Series
9/22/2015	Gino Cingolani	Liesbeth Veenhoff	Structural basis for recognition of import substratesStructural basis for recognition of import substrates	Thomas Jefferson University, Philadelphia	Extra Seminar ERIBA
10/25/2015	Claus Azzalin	Ageing Meeting	Terra, cellular senescence and immortality in fission yeast and human cells	Institute of Biochemestry, Zürich, Suisse	Molecular Biology of Ageing 2015
10/25/2015	Daniel Gottschling	Ageing Meeting	Wrestling with understanding how interconnected biological systems change with age	FHCRC, Seattle, USA	Molecular Biology of Ageing 2015
10/25/2015	Lea Harrington	Ageing Meeting	The telomere Goldilocks effect: the disadvantages of telomeres that are very short or very long	University of Montreal, Canada	Molecular Biology of Ageing 2015
10/25/2015	Karl Lenhard Rudolph	Ageing Meeting	Hoxa9 induced developmental signals impair muscle stem cells and muscle regeneration in ageing mice	Leibniz Institute for Age Research, Jena, Germany	Molecular Biology of Ageing 2015
10/26/2015	Niels de Wind	Ageing Meeting	Endogenous DNA damage, replication stress, and ageing	Leiden University Medical Center, the Netherlands	Molecular Biology of Ageing 2015
10/26/2015	Andres Aguilera	Ageing Meeting	The role of chromatin in R-loop and transcription-mediated genome instability	University of Seville, Spain	Molecular Biology of Ageing 2015
10/26/2015	Vilhelm Bohr	Ageing Meeting	Nuclear to mitochondrial DNA damage signaling	National Institutes of Health, Baltimore, USA	Molecular Biology of Ageing 2015
10/26/2015	Anja Groth	Ageing Meeting	Chromatin replication and epigenome maintenance	University of Copenhagen, Denmark	Molecular Biology of Ageing 2015
10/26/2015	Alexandra Zhernakova	Ageing Meeting	Understanding the biology of ageing by co-expression analysis of genes differentially expressed with age	University of Groningen, the Netherlands	Molecular Biology of Ageing 2015
10/26/2015	Riekelt Houtkooper	Ageing Meeting	Mitochondria in the control of metabolism and ageing	AMC Amsterdam, the Netherlands	Molecular Biology of Ageing 2015
10/26/2015	Takehiko Kobayashi	Ageing Meeting	rDNA stability determines the fate of cell	The University of Tokyo	Molecular Biology of Ageing 2015

Date	External invited Speakers	Host	Title	Institute	Event
10/26/2015	Björn Schumacher	Ageing Meeting	DNA Damage Responses during Development and Ageing	University of Cologne, Germany	Molecular Biology of Ageing 2015
10/26/2015	John Sedivy	Ageing Meeting	Epigenetic changes and somatic retrotransposition in mammalian ageing	Brown University, Rhode Island, USA	Molecular Biology of Ageing 2015
10/26/2015	Jan Vijg	Ageing Meeting	Genome instability: A conserved mechanism of ageing?	Albert Einstein College of Medicine. New York, USA	Molecular Biology of Ageing 2015
10/26/2015	Lene Rasmussen	Ageing Meeting	Interplay between translesion synthesis and mitochondrial function in mammalian cells	University of Copenhagen, Denmark	Molecular Biology of Ageing 2015
10/26/2015	João Passos	Ageing Meeting	Mitochondria are required for pro-ageing features of the senescent phenotype	Newcastle University, UK	Molecular Biology of Ageing 2015
10/26/2015	Steve Jackson	Ageing Meeting	Potential therapy for a human premature ageing disease identified through cell-based screens	University of Cambridge, UK	Molecular Biology of Ageing 2015
10/27/2015	Holly Brown - Borg	Ageing Meeting	Impact of growth hormone on metabolism and the epigenome in ageing	University of North Dakota, USA	Molecular Biology of Ageing 2015
10/27/2015	Christoph Englert	Ageing Meeting	*Nothobranchius furzeri*: A short-lived killifish as a new model for age research	Fritz Lipmann Institute, Jena, Germany	Molecular Biology of Ageing 2015
10/27/2015	Thorsten Hoppe	Ageing Meeting	The Quality Control Ubiquitin Ligase CHIP Couples Proteostasis and Ageing Through Insulin Receptor Degradation	CECAD Cologne, Germany	Molecular Biology of Ageing 2015
10/27/2015	Judith Frydman	Ageing Meeting	Pathways of Quality Control; Protein folding and misfolding in the eukaryotic cytosol	Stanford University, USA	Molecular Biology of Ageing 2015
10/27/2015	Jorg Goronzy	Ageing Meeting	The chromatin landscape in T cell ageing	Stanford University, USA	Molecular Biology of Ageing 2015
10/27/2015	Karim Mekhail	Ageing Meeting	Caloric Restriction in the Suppression of Destructive RNA-DNA Marriages and Identification of Molecular DNA Ambulances	University of Toronto, Cananda	Molecular Biology of Ageing 2015
10/27/2015	Michael Milsom	Ageing Meeting	Hematopoietic stem cell decline driven by stress-induced DNA damage	HI-STEM and DKFZ, Heidelberg, Germany	Molecular Biology of Ageing 2015

Date	External invited Speakers	Host	Title	Institute	Event
10/27/2015	Thomas Nystrom	Ageing Meeting		University of Gothenburg, Sweden	Molecular Biology of Ageing 2015
10/27/2015	Scott Pletcher	Ageing Meeting	Neuronal control of ageing in Drosophila	University of Michigan, Detroit, USA	Molecular Biology of Ageing 2015
10/27/2015	Yousin Suh	Ageing Meeting	Functional genomics approach to develop targets for slowing ageing in humans	Albert Einstein College of Medicine, New York, USA	Molecular Biology of Ageing 2015
10/28/2015	Judith Campisi	Ageing Meeting	Cellular senescence: Yin and Yang	Buck Institute for Research on Ageing, Novato, USA	Molecular Biology of Ageing 2015
10/28/2015	Jan van Deursen	Ageing Meeting	Senescence pathways in ageing and age-related disease	Mayo Clinic, Rochester, USA	Molecular Biology of Ageing 2015
10/28/2015	Marc van de Wetering	Ageing Meeting		Hubrecht Institute, Utrecht, the Netherlands	Molecular Biology of Ageing 2015
10/28/2015	Katarzyna Siudeja	Ageing Meeting	Frequent somatic mutation drives neoplasia and genetic mosaicism in ageing adult intestinal stem cells	Institut Curie, Paris	Molecular Biology of Ageing 2015
10/29/2015	Jacco van Rheenen	Floris Foijer	Intravital imaging of tumor heterogeneity and plasticity	Hubrecht Institute Utrecht, The Netherlands	Molecular Medicine Series
11/5/2015	Grant W. Brown	Michael Chang	Dissecting the DNA replication stress response with functional genomics	Dept. Of Biochemistry, University of Toronto / Donnelly Centre for Cellular and Biomolecular Research Toronto, Canada	Molecular Medicine Series
11/6/2015	J.J. Schuringa	Liesbeth Veenhoff	Towards identification and targeting of leukemic stem cells	Dept. Of Hematology, UMCG. Groningen, The Netherlands	Friday Afternoon Meeting
11/21/2015	Martijn Nolte	Gerald de Haan	The cells that rock the cradle: The impact of T cells on blood cell formation	Sanquin, Amsterdam, The Netherlands	Extra ERIBA Seminar
12/4/2015	Puck Knipscheer, doctoral student	Peter Lansdorp	When DNA replication runs into problems'	Hubrecht Institute, Utrecht	Extra ERIBA seminar

Date	External invited Speakers	Host	Title	Institute	Event
12/4/2015	Bastiaan Evers	Floris Foijer	High-throughput screening technologies to find synthetic lethal interactions	Netherlands Cancer Institute, Amsterdam, The Netherlands	Friday Afternoon Meeting
12/10/2015	Roderick Lim	Liesbeth Veenhoff	Selective transport through the nuclear pore complex	Biozentrum University of Basel, Basel, Swiss	Extra ERIBA Seminar
1/28/2016	Miguel Godinho Ferreira	Michael Chang	The role of telemores in cancer and ageing in zebrafish	Gulbenkian Science Institute, Oeiras, Portugal	Molecular Medical Series
2/4/2016	Edwin Cuppen	Peter Lansdorp	Genetic integrity of adult stem cells	Dept. of Genetics, UMC Utrecht, the Netherlands	Molecular Medical Series
2/5/2016	prof. dr. M.A.T.M. (Marcel) van Vugt	Michael Chang	Dealing with DNA damage throughout the cell cycle	Faculty of Medical Sciences, Medical Oncology, UMCG, Groningen, the Netherlands	Friday Afternoon Meeting
3/17/2016	Joao Passos	Marco Demaria	Telomeres and mitochondria. Guardians of senescence	Newcastle University Institute for Ageing, Newcastle, UK	Molecular Medical Series
3/24/2016	Douglas Higgs	Gerald de Haan	Understanding α-globin gene regulation and implications for the treatment of ß-thalassemia	Weatherall Institure of Molecular Medicine, University of Oxford, Headington, Oxford, UK	Molecular Medical Series
3/30/2016	Hans Clevers	Gerald de Haan	Lgr5 stem cell-grown organoids and their applications	Hubrecht Institute for Developmental Biology/Princess Maxima Center for Pediatric Oncology	Molecular Medical Series
4/1/2016	Tjakko J. van Ham, doctoral student	Ellen Nollen	Towards functional genomics of brain macrophage development and function	Department of Clinical Genetics Erasmus MC, Rotterdam, the Netherlands	Friday Afternoon Meeting
4/21/2016	Jesus Gil	Marco Demaria	Linking senescence and inflammation: the senescene-associated secretory phenotype (SASP)	Imerial College London, Institute of Clinical Science, London, UK	Molecular Medical Series
4/28/2016	Steven Pollard	Floris Foijer/ Daniël Warmer-dam	Genome editing in mammalian neural stem cells	MRC Centre for Regenerative Medicine, The University of Edinburgh, UK	Molecular Medical Series

Date	External invited Speakers	Host	Title	Institute	Event
5/26/2016	Kara Bernstein	Michael Chang	Uncovering mechanisms of error free DNA repare and cancer	Bernstein Laboratory, University of Pittsburgh, USA	Molecular Medical Series
6/23/2016	Jacqueline Jacobs	Michael Chang			ERIBA retreat
6/23/2016	Luigi Fontana	Marco Demaria	Promoting Health and Longevity trough Diet: metabolic and molecular mechanisms	Brescia University, Italy ; Washington University, USA	Molecular Medical Series
9/2/2016	John Barker	Eugene Berezikov	From transplanting to regrowing hands and faces	J.W. Goethe-Universität, Frankfurt	Friday Afternoon Meeting
9/8/2016	Michael Platten	Ellen Nollen	Metabolic Control	Neurology Clinic, University of Mecical Centre Heidelberg, Germany	Molecular Medical Series
9/9/2016	Susanne Kooistra	Gerald de Haan	Biological and molecular functions of the Jmjd2 histone demethylases	Department of Neuroscience van het UMCG	Friday Afternoon Meeting
9/22/2016	René Ketting	Eugene Berezikov	Small RNA mediated silencing within and across generations	Institute Molecular Biology, Mainz, Germany	Molecular Medical Series
9/22/2016	Sietske Bakker	Daniël Warmer-dam	Genome maintenance strategies in hematopoietic stem cells	Passegué laboratory, The Eli and Edythe Broad Center of Regeneration Medicine and Stem Cell Research, UCSF, San Francisco, USA	Seminar at ERIBA
10/7/2016	Steven Bergink	Katrin Paeschke	genome maintenance and protein quality control	UMCG, Celbiologie	Friday Afternoon Meeting
10/11/2016	Philippe Joanin	Diana Spierings	ICELL8 Single-Cell System for single-cell RNA-seq studies	Wafergen	Seminar at ERIBA
10/13/2016	Rob Wolthuis	Floris Foijer	The Control of Sister Chromatid Cohesion in Normal and Cancer Cells	Dept. Of Oncogenetics, VUmc Cancer Center, Amsterdam	Molecular Medical Series
10/25/2016	Shay Geula	Eugene Berezikov	Deciphering the molecular role of N6-Methyladenosine mRNA modification in distinct pluripotent states and the development of mammalian embryo	Weizmann Institute of Science, Israel	Seminar at ERIBA

Date	External invited Speakers	Host	Title	Institute	Event
11/10/2016	Andrea Alimonti	Marco Demaria	Non-Cell-Autonomous Regulation of Cellular Senescence in Cancer	Institute of Oncology Research (IOR) Bellinzona, Switzerland	Molecular Medical Series
11/30/2016	Puck Knipscheer	Peter Lansdorp	Studying G-quadruplex unwinding during DNA replication in Xenopus egg extracts	Hubrecht Laboratory, Utrecht	Seminar at ERIBA
11/30/2016	Marcel Tijsterman	Peter Lansdorp	First and second line of defense against G-quadruplexes	UMC Leiden	Seminar at ERIBA
11/30/2016	Julian Sale	Peter Lansdorp	Monitoring the replication of G-quadruplexes in vivo	MRC Laboratory of Molecular Biology, Cambridge, UK	Seminar at ERIBA
12/1/2016	Rachel Eiges	Peter Lansdorp	Understanding the epigenetics of untranslated repeat expansion disorders using mutant pluripotent stem cells	Medical Genetics Institute Shaare Zedek Medical Center Jerusalem, Israel	Seminar at ERIBA
12/8/2016	Katherine Marcelain	Floris Foijer	The Ski protein: from transcriptional repression to genomic stability maintenance	University of Chile	Seminar at ERIBA

10. Governance and Management

10. Governance and Management

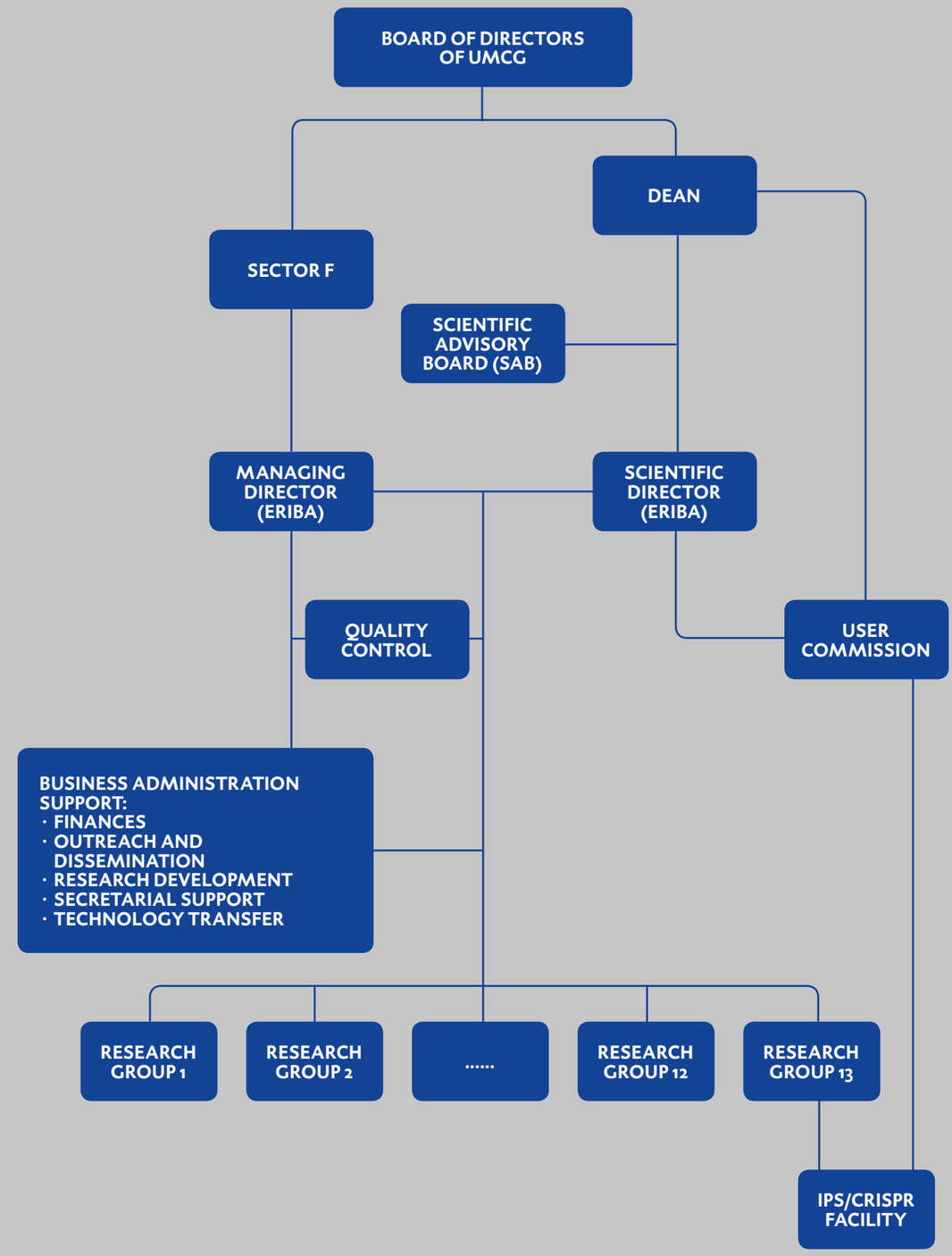
ERIBA is managed by the Head of the Department of the Biology of Ageing (Gerald de Haan), who serves as Scientific Director, and the Managing Director (Henk Heidekamp). The Head of the Department, appointed by the Board of Directors of UMCG, is responsible for leading the Department's overall work in relation to science and strategy. The Managing Director is responsible for the daily management, which includes the coordination of all financial and Human Resource matters.

The Management Team also comprises representatives of the Principal Investigators who rotate every two years, and a representative of the Research Development Office. Their mandate is regulated by the Head of the Department and the Managing Director and they assist the Directors by providing advice on policy and administration relating to their area of responsibility.

The Department is embedded in Sector Development and Transfer of the UMCG, which controls the administration and supports the management of the Department.

The organizational chart illustrates ERIBA's governance structure.

DEPARTMENT OF THE BIOLOGY OF AGEING



11. Scientific Advisory Board

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The role of the ERIBA Scientific Advisory Board is to provide advice on institutional strategy, recruitment, viability, and on past performance and future potential of individual investigators and research programs. The Members of the Board will conduct in-depth reviews of ERIBA's research programs each year and will aid ERIBA and UMCG leadership to ensure its programs meet the highest international standards and achieve optimal scientific impact.

The Board is comprised of the following distinguished scientists:

Jan Hoeijmakers
Professor of Molecular Genetics
Institute of Genetics
Erasmus Medical Center Rotterdam
The Netherlands

Christine Mummery
Professor of Developmental Biology
Chair of the Department of Anatomy and Embryology
Leiden University Medical Center
The Netherlands

Johan Auwerx
Professor and Nestlé Chair in Energy Metabolism
Ecole Polytechnique Fédérale in Lausanne
Switzerland

Yves Barral
Associate Professor of Biochemistry
Department of Biology
ETH Zurich
Switzerland

Helle Ulrich
Scientific Director of the Institute of Molecular Biology
Professor at the Faculty of Biology
University of Mainz
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