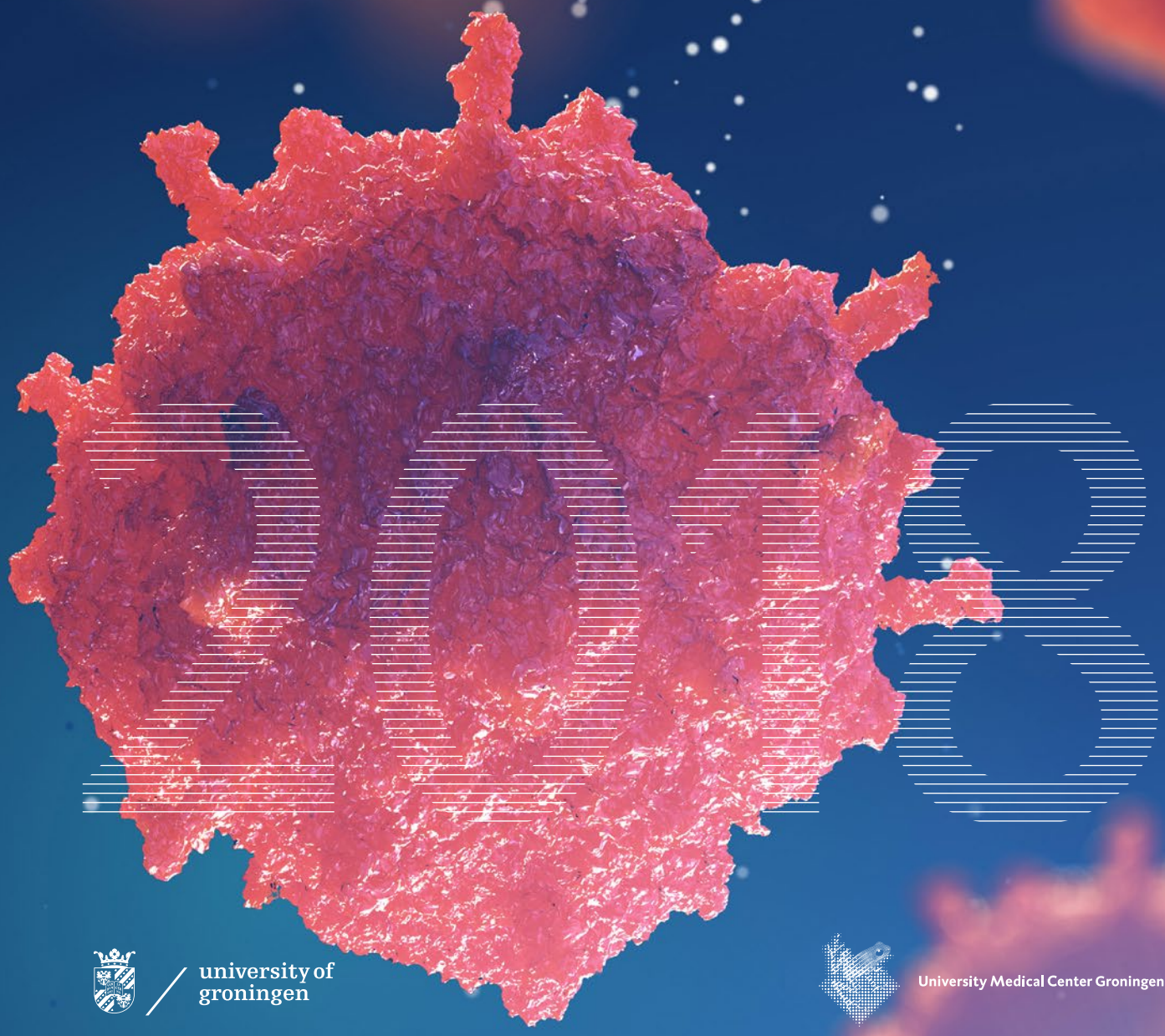
ERIBA

European Research Institute for the Biology of Ageing

Annual Report 2018



university of groningen

University Medical Center Groningen

Annual Report 2018

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ERIBA

www.eriba.umcg.nl

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Foreword
2018 in review

It is a great pleasure to present to you the 2018 Annual Report of the European Research Institute for the Biology of Ageing. This report provides you with an overview of all our activities and achievements, in science, education, business development and outreach. We value all these domains equally and are proud to share with you all that has been accomplished in 2018.

We published a record number of 58 papers, the large majority of which were the result of teams of ERIBA scientists collaborating with each other, or with researchers outside our Institute. More than 30% of our publications originate from collaborations with Departments in the UMCG or in the Faculty of Science and Engineering at the University of Groningen. In December, ERIBA and the Institute for Molecular Biology in Mainz, Germany, organized a joint retreat to explore novel collaborative projects between our two Institutes. We believe that collaboration in science, where multiple teams work towards a single goal, is required to reach our purpose: the discovery of critical mechanisms of ageing and age-related diseases and the development of new intervention strategies.
We are very committed to contributing to talent development in the field of ageing research. In 2018 many highly talented PhD students joined our training program, and similarly, undergraduate students enrolled at Universities from all over the world have come to ERIBA. It is particularly satisfying to see that many biomedical students have a keen interest in ageing research, and carry out rotations in our Institute.

We are also very proud that in 2018 ERIBA's first spin-off company Cleara Biotech BV was launched, co-founded by one of our researchers, Marco Demaria. Cleara Biotech aims to develop and optimize therapeutics to treat patients with a range of disease caused by a failure to clear senescent cells.
Progress in science is exponential, and it is of imminent importance to share our findings with society. In 2018 ERIBA scientists were involved in many of such

It is satisfying to see that the University of Groningen MSc Track in Biology of Ageing has become very popular, and many of the students from this Track carry out rotations in our Institute.

outreach activities. One noted example was the development of a toolbox allowing high school students to perform experiments to study regeneration in their own classroom. We hosted many delegations from Dutch Ministries, foreign Universities, private companies, and Embassies, including visits from the Ambassador of India, Germany and of the United States. In all these meetings we experienced excitement when we share our ambition to prevent, delay, or reverse aspects of the ageing process.

Looking forward to 2019, we anticipate to continue and expand collaborative scientific research projects aimed to identify biological ways to prevent age-related diseases. This will include collaborations between different ERIBA research teams, and with many scientists outside ERIBA. One of our priorities will be to find resources and funding opportunities to finance such collaborations. These funding opportunities may well reside in programs in which we partner with private entities.

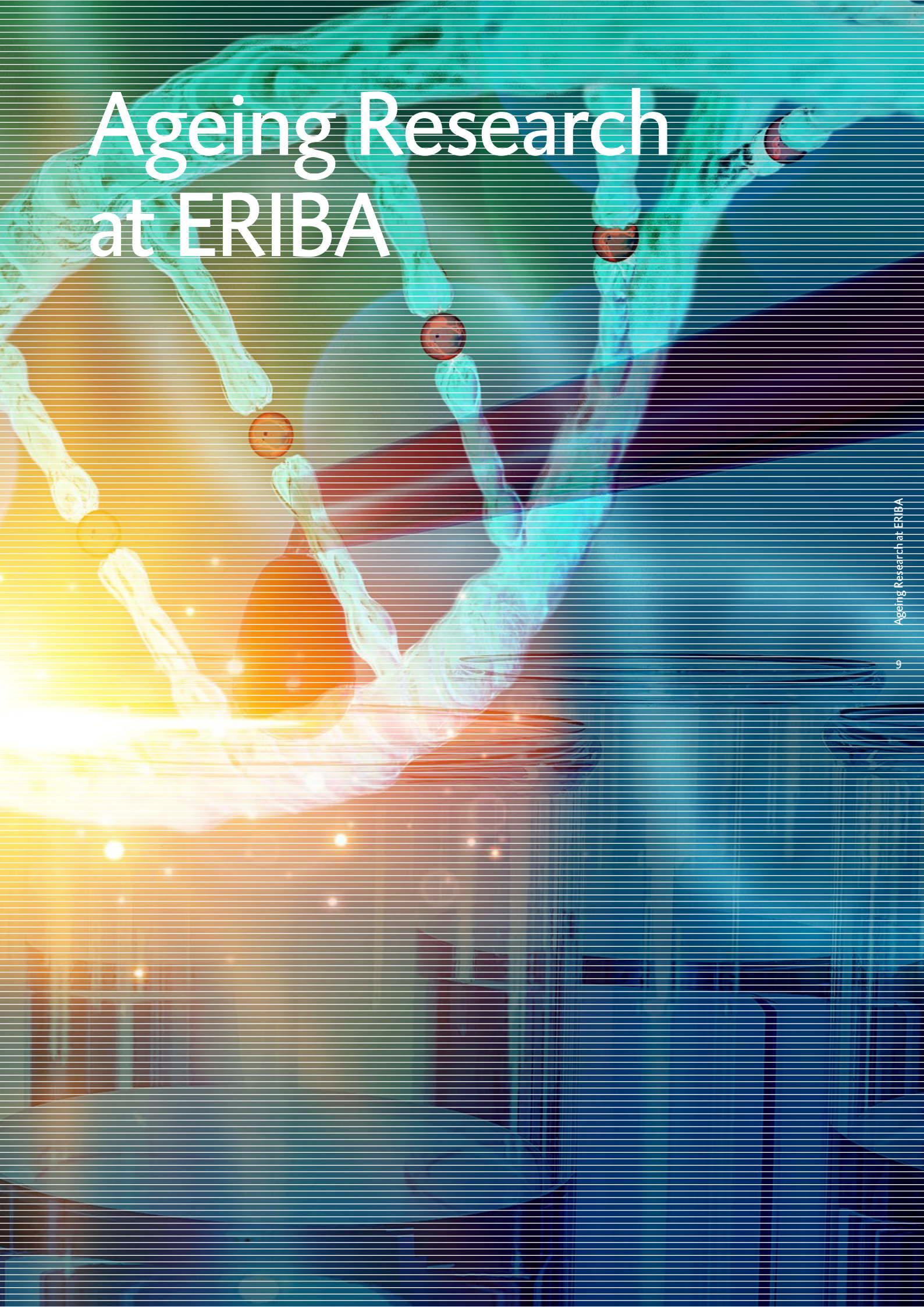
In 2018 one of our researchers, Katrin Paeschke, left us after accepting a new Chair position in Bonn. While we are sad to see Katrin leave, at the same we are proud to see that ERIBA scientists are recruited to other prestigious institutes. This is also true for PhD students who have graduated in ERIBA. Without exception, they find excellent positions elsewhere and thus contribute to our alumni network. Importantly, we expect the arrival of a new ERIBA scientist in the summer of 2019.

In October 2019 we will continue our highly successful biennial conference series on the Molecular Biology of Ageing with a third meeting in Groningen. We have assembled a stellar team of international speakers and are very much looking forward to hosting our scientific colleagues later this year.

I believe we are well underway to achieve our ambition, to become a globally leading institute for innovative research on the biological mechanisms of ageing.

Gerald de Haan
Scientific Director
February 2019

Ageing Research at ERIBA



Ageing Research at ERIBA

ERIBA is an internationally recognised European research centre on ageing. The institute focuses on fundamental biology to understand the causes of ageing. At ERIBA, studies are focused on the mechanisms that result in the loss of cells with age, and decline in function of old cells and tissues.

Discoveries at ERIBA explain ageing phenomena such as stem cell loss of function, genome instability, loss of protein homeostasis, and metabolic decline. These phenomena are at the root of age-related frailty and major age-related diseases, such as cancer, neurodegeneration, and diabetes.

ERIBA aims to develop novel strategies to prevent or combat age-related diseases and to provide evidence-based recommendations for healthy ageing. ERIBA's approach is to deliver new drug targets, specialized models, and assays for the purpose of adding more healthy years to human life.

Stem Cell Regulation and Mechanisms of Regeneration
The Laboratory led by Eugene Berezikov aims at understanding molecular mechanisms that regulate regeneration and activity of stem cells.

Gene Regulation In Ageing and Age-Related Diseases
The group of Cor Calkhoven is particularly interested in the function of mRNA control elements, protein factors and microRNAs that are involved in mTORC1-controlled processes.

Telomeres and Genome Integrity
The overall goal of Michael Chang's Laboratory is to figure out the mechanisms used by a cell to protect its genome from becoming mutated or inappropriately altered or rearranged.

Genomic Instability in Development and Disease

The long-term aim of the Laboratory of Floris Foijer and his team is understanding aneuploidy to improve cancer therapy.

Quantitative Epigenetics

The group of Maria Colomé-Tatché is interested in understanding the epigenetic changes that take place during the processes of development, ageing and disease.

Nucleic Acids Structures and Repair

The particular focus of Katrin Paeschke Laboratory is to understand the nature and role of secondary structures that form within nucleic acids.

Genome Structure Ageing

Research at the Laboratory of Victor Guryev is aimed at understanding structural changes in human genomes for a better detection of genomic and environmental risks as well as for disease prevention.

Ageing Biology and Stem Cells

The aim of studies of Gerald de Haan's Laboratory is to understand the mechanisms that specify normal hematopoietic stem cell functioning from birth to death.

Asymmetric Cell Division and Ageing

Judith Paridaen and her group are focused on understanding how microscopic processes within single stem cells affect their function which is essential to answer how stem cells shape and can help to maintain an healthy body.

Genetic Instability and Ageing

The role of genome instability in stem cells in relation to disease processes and ageing is the main focus of Peter Lansdorp group.

Cellular Senescence and Age-related Pathologies

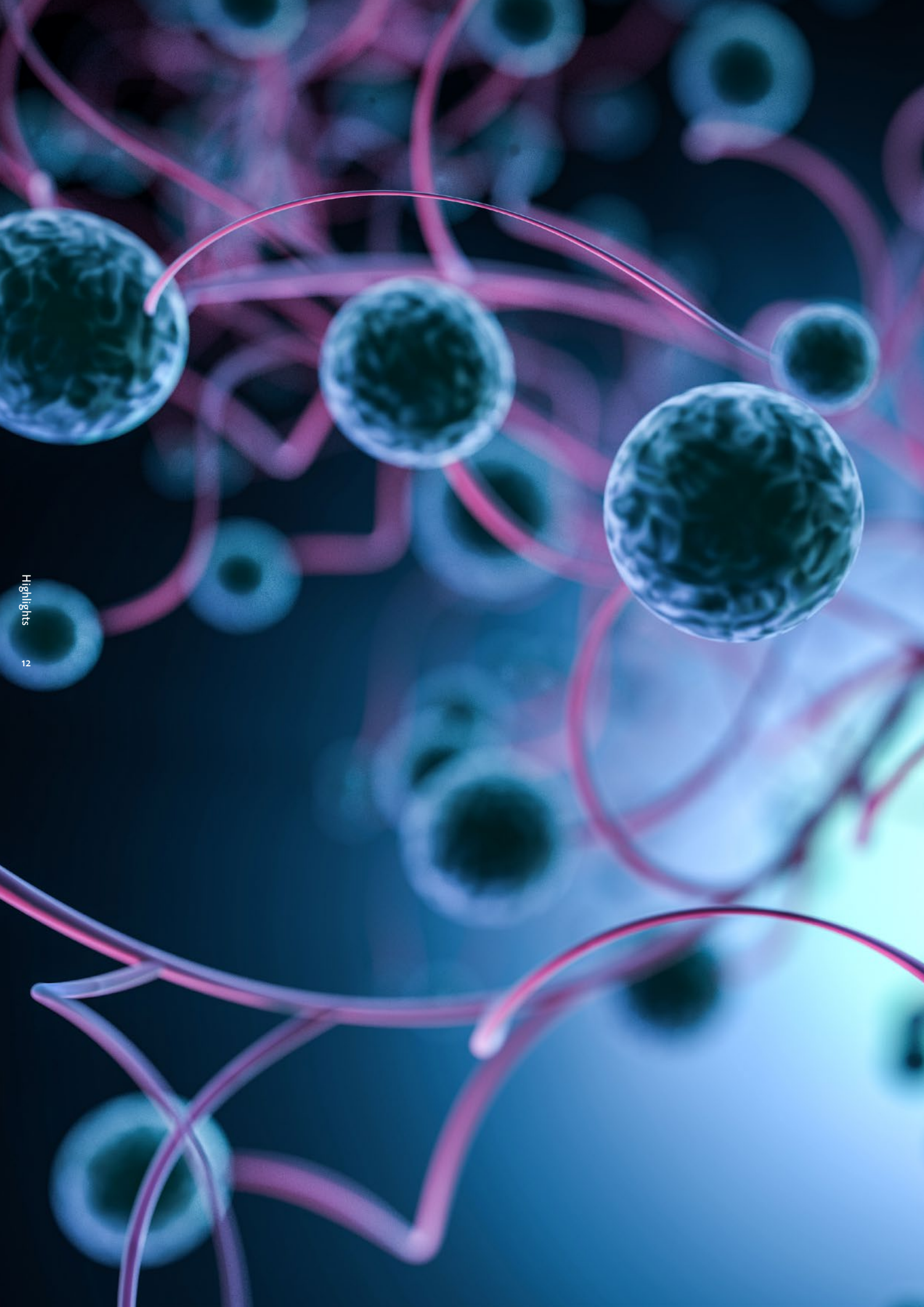
Marco Demaria's Group aims to understand the basic molecular and cellular mechanisms of ageing, particularly a specific cellular state, "senescence".

Cellular Biochemistry

The laboratory of Liesbeth Veenhoff aims for a system wide global characterization of age-related changes, as well as detailed understanding how the NPCs and cognate transport factors play a role in cellular ageing.

Molecular Neurobiology of Ageing

The group led by Ellen Nollen is focused on understanding the molecular mechanisms that drive age-related toxicity of aggregation-prone proteins, which plays a role in age-related diseases like Parkinson and Alzheimer.



2018 Highlights

2018 Highlights

This section reports a selected number of achievements that have been accomplished by ERIBA staff in 2018.

Scientific Publications

In 2018, ERIBA scientists published a record number of 58 papers in scientific journals. Many of the published papers were the result of fruitful collaborations. Joint projects were initiated between research groups in ERIBA, between scientists in ERIBA with research groups at the University Medical Center Groningen and the Faculty of Science and Engineering of the University of Groningen, and with international partners.

ERIBA researchers in the groups of **Michael Chang** and **Liesbeth Veenhoff** developed a high-throughout, genome-wide approach to identify genes that suppress the accumulation of mutations during ageing using yeast as a model organism. In addition to identifying a number of new genes that counteract the accumulation of mutations independently of age, they discovered that PEX19, a gene involved in the biogenesis of peroxisomes is important to prevent the accumulation of mutations in aged cells.

> Novarina D, Janssens G, Bokern K, Schut T, van Oerle N, Kazemier HG , Veenhoff LM & Chang M. (2018). *A genome-wide screen identifies genes that suppress the accumulation of spontaneous mutations in young and aged yeast cells*. bioRxiv. DOI: 10.1101/492587

The **Calkhoven** group showed that repression of a protein known as LIP by a calorie restricted diet is involved in slowing the ageing process and increasing healthy life expectancy. They generated mice that are deficient in LIP and demonstrated that these mice are leaner, metabolically healthier, physically fitter and more resistant to cancer than normal mice. The study was performed in collaboration with a scientist from the German Leibniz Institute on Ageing (Fritz Lipmann Institute) and scientists from the UMCG.

> Müller C, Zidek LM, Ackermann T, de Jong T, Liu P, Kliche V, Zaini MA, Kortman G, Harkema L, Verbeek DS, Tuckermann JP, von Maltzahn J, de Bruin A, Guryev V, Wang ZQ, Calkhoven CF. *Reduced expression of C/EBPβ-LIP extends health- and lifespan in mice.* Elife. 2018 DOI: 1 0.7554/eLife.34985

In collaboration with Elsa Logarinho in Porto, the **Foijer's** lab found that chromosome segregation fidelity decreases with age. This resulted from decreased expression of several mitotic proteins and is instigated by the transcription factor FoxM1. Importantly, reconstitution of FoxM1 in aged human fibroblasts improved mitotic fidelity, suggesting that reactivation of FoxM1 in old tissues might decrease ageing phenotypes.

> Macedo JC, Vaz S, Bakker B, Ribeiro R, Bakker PL, Escandell JM, Ferreira MG, Medema R, Foijer F, Logarinho E. *FoxM1 repression during human aging leads to mitotic decline and aneuploidy-driven full senescence.* Nat Commun. 2018 Jul 19;9(1):2834.

Eugene Berezikov's group discovered that the regenerative flatworm Macrostomum lignano can live surprisingly long, and the analysis of gene expression changes with age suggests that M. lignano has evolved molecular mechanisms for offsetting negative consequences of ageing, making it a novel powerful model for the exploration of anti-ageing strategies.

> Mouton S, Grudniewska M, Glazenburg L., Guryev V, Berezikov E. (2018). *Resilience to aging in the regeneration-capable flatworm Macrostomum lignano.* Aging Cell 2018; e12739.

Victor Guryev's group collaborated with researchers from several UMCG departments to characterize medulloblastoma tumor subgroups at phospho-protein-signaling level. Their findings may hold a key for new therapeutic targets.

> Zomerman WW, Plasschaert SLA, Conroy S, Scherpen FJ, Meeuwsen-de Boer TGJ, Lourens HJ, Guerrero Llobet S, Smit MJ, Slagter-Menkema L, Seitz A, Gidding CEM, Hulleman E, Wesseling P, Meijer L, van Kempen LC, van den Berg A, Warmerdam DO, Kruyt FAE, Foijer F, van Vugt MATM, den Dunnen WFA, Hoving EW, Guryev V, de Bont ESJM, Bruggeman SWM. *Identification of Two Protein-Signaling States Delineating Transcriptionally Heterogeneous Human Medulloblastoma.* Cell Rep. 2018 Mar 20;22(12):3206-3216.

Gerald de Haan's group collaborated with scientists in Germany in a study in which they demonstrate that it is possible to predict the chronological age of a mouse by assessing the DNA methylation pattern of only 3 genomic loci in peripheral blood cells.

> Han Y, Eipel M, Franzen J, Sakk V, Dethmers-Ausema B, Yndriago L, Izeta A, de Haan G, Geiger H, Wagner W. *Epigenetic age-predictor for mice based on three CpG sites.* Elife. 2018; doi: 10.7554/eLife.37462.

Ellen Nollen's group collaborated with a scientist in the UK to develop a platform that allows for the automated analysis of movements and behavior of the nematode C.elegans, a model organism that is frequently used as a model for human ageing. This tracker platform allows to comprehensively and rapidly screen for mechanisms of age-related functional decline and age-related diseases.

> Perni M, Challa PK, Kirkegaard JB, Limbocker R, Koopman M, Hardenberg MC, Sormanni P, Müller T, Saar KL, Roode LWY, Habchi J, Vecchi G, Fernando N, Casford S, Nollen EAA, Vendruscolo M, Dobson CM, Knowles TPJ. *Massively parallel C. elegans tracking provides multi-dimensional fingerprints for phenotypic discovery.* J Neurosci Methods. 2018 Aug 1;306:57-67.

Liesbeth Veenhoff's group studies nuclear pore complexes, the conserved gates to the nucleus, and one of the largest molecular machines in cells. Her team showed that assembly of new nuclear pore complexes frequently fails in aged cells, and consequently, transport and communication between the nucleus and cytosol is impaired.

> Irina L Rempel, Matthew M Crane, Ankur Mishra, Daniel PMJansen, Georges Janssens, Petra Popken, Matt Kaeberlein, Erik van der Giessen, Patrick Onck, Anton Steen, Liesbeth M. Veenhoff. *Age-dependent deterioration of nuclear pore assembly in mitotic cells decreases transport dynamics*. bioRxiv 477802; doi: https://doi.org/10.1101/477802.

Patients with Bloom syndrome show accelerated ageing. The protein that is defective in Bloom syndrome is important to prevent genome instability and cells from Bloom syndrome patients show frequent exchanges of DNA strands between sister chromatids. **Peter Lansdorp's** group mapped the location of such DNA exchanges onto chromosomes. Strikingly, the exchanges were found to be enriched at active genes, especially if the genes had sequence motifs predicted capable of forming stable secondary structures known as guanine quadruplex structures.

> van Wietmarschen N, Merzouk S, Halsema N, Spierings DCJ, Guryev V, Lansdorp PM. *BLM helicase suppresses recombination at G-quadruplex motifs in transcribed genes*. Nat Commun. 2018 Jan 18;9(1):271.

Judith Paridaen contributed to a study revealing how neurons are generated during embryonic development of the mouse brain. In this publication, the molecular mechanism underlying the migration of newborn neural progenitors away from their initial position close to the brain ventricle was elucidated.

> Tavano S, Taverna E, Kalebic N, Haffner C, Namba T, Dahl A, Wilsch-Bräuninger M, Paridaen JTML, Huttner WB. *Insm1 Induces Neural Progenitor Delamination in Developing Neocortex via Downregulation of the Adherens Junction Belt-Specific Protein Plekha7*. Neuron. 2018 Mar 21;97(6):1299-1314.

Marco Demaria's group has characterized the induction and accumulation of cellular senescence in the colon mucosa of humans and mice under conditions of calorie restriction (CR). Surprisingly, they measured strongly decreased levels of senescent cells in CR, suggesting that the beneficial effects of reducing calorie intake might be partly due to prevention of senescence.

> Fontana L, Mitchell SE, Wang B, Tosti V, van Vliet T, Veronese N, Bertozzi B, Early DS, Maissan P, Speakman JR, Demaria M. *The effects of graded caloric restriction: XII. Comparison of mouse to human impact on cellular senescence in the colon*. Aging Cell. 2018 Jun;17(3):e12746

Grants

In 2018 ERIBA secured € 3.3 million from grants. This included prestigious grants from the EU and from the Dutch Cancer Society. The institute also received private funding from Cleara Biotech B.V., ERIBA's first startup company. Detailed information about ERIBA grants and funding can be found on page 28.

Awards

The UMCG annual research innovation award was granted to **Diana Spierings** for her approach to identify genetic changes in individual cells.

Judith Paridaen was awarded a travel grant from EuFishBiomed to attend the 5th European Zebrafish Principal Investigator Meeting in Trento, Italy.

Former ERIBA PhD student **Clémence Claussin** was awarded an EMBO Long Term Fellowship. Clémence is currently a postdoc at the Memorial Sloan Kettering Cancer Center in New York.

Glòria Casas Gimeno received a poster prize at the International FishMed Conference held in Warsaw, Poland.

Graduations

In 2018, eight scientists graduated from ERIBA as PhD students and since have moved to their next position: **Judith Simon** (Floris Foijer Lab, currently at Bart's Cancer Institute London, UK), **Sonia Stinus** (Michael Chang Lab, now at Laure Crabbé, Toulouse, F), **Tobias Ackermann** (Cor Calkhoven Lab, now at Beatson Institute, Glasgow, UK), **Seka Lazare** (Gerald de Haan Lab, now at Illumina Inc, San Diego, CA, USA), **Johannes Jung** (Gerald de Haan Lab, now at University Hospital, Freiburg, DE), **Esther Stroo** (Ellen Nollen Lab, now at Catalyze, Amsterdam, NL), **Aaron Taudt** (Maria Colomé Tatché Lab, now at QuantIP, Munich, DE), **Ilke Sen** (Christian Riedel Lab, now at Karolinska Institute, Sweden), **Jakub Wudarski** (Eugene Berezikov Lab, now a Postdoctoral fellow in ERIBA).

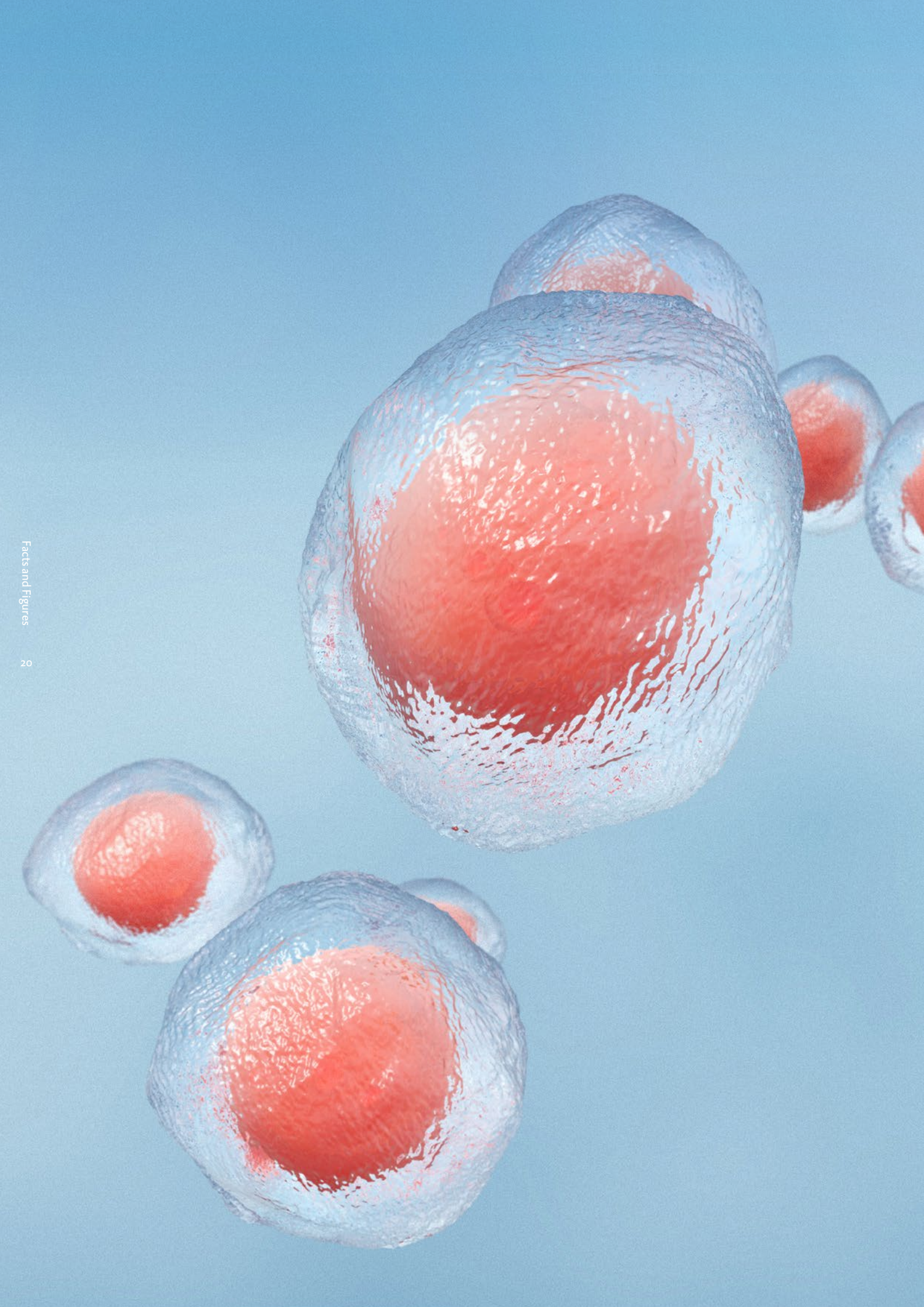
Scientific Dissemination and Public Outreach

Members of the ERIBA Outreach Committee organized the first Career Day on March 14th, 2018 with contributions from former PhD students now employed by industry or university. More than 70 PhD students and postdocs from ERIBA and the UMCG attended this inspiring meeting.

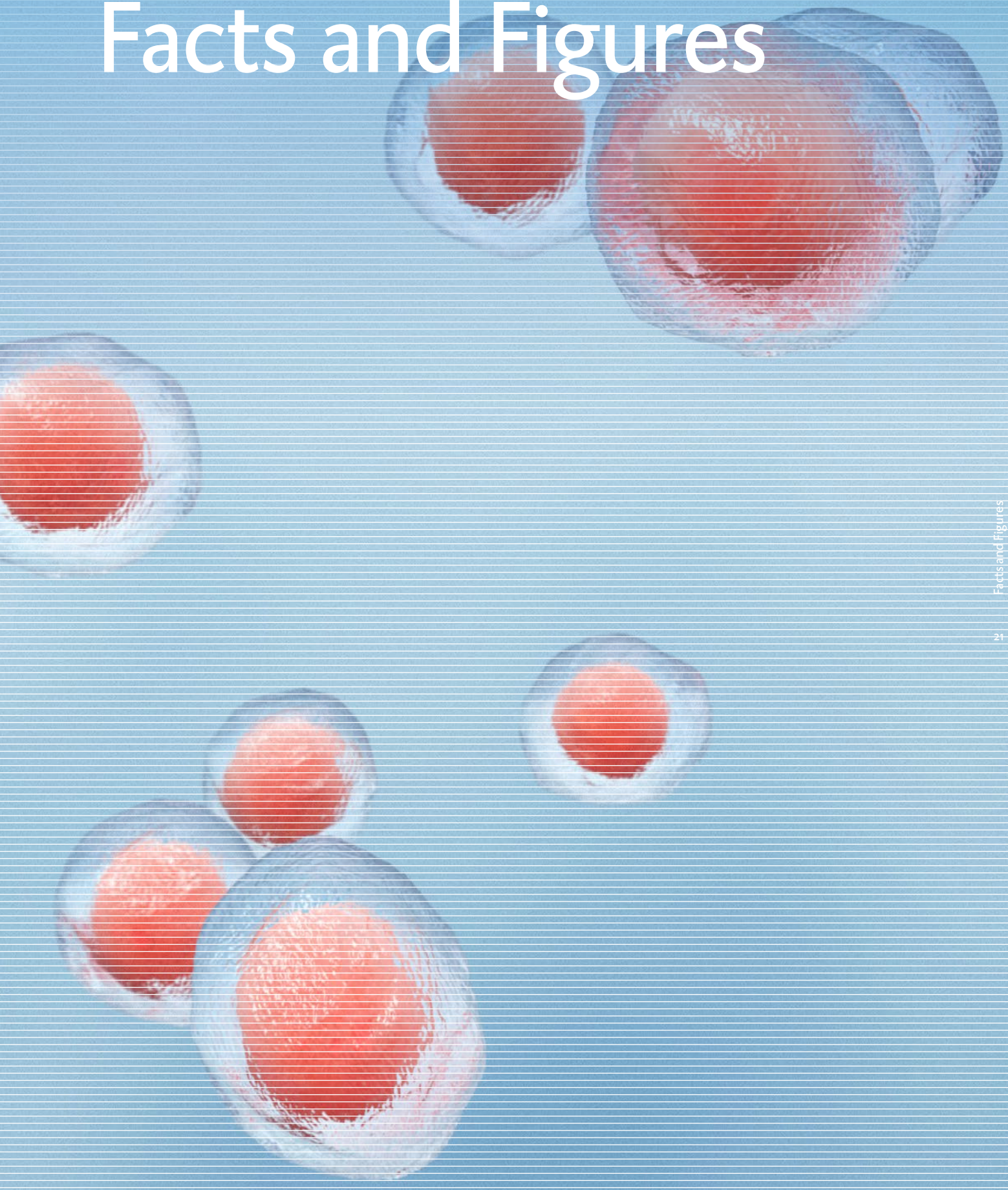
ERIBA scientists were actively involved in many outreach activities. We opened our doors to the general audience to share our excitement for science at the **Zpannend Zernike** event, and hosted approximately 700 people.

There is an ongoing and important discussion on the use of lab animals for experimentation. Some protestors wish for all animal experiments to stop immediately. However, currently, many animal experiments are still performed in the Netherlands and elsewhere. Why do we still need experimental animals, and how are they treated? Are there alternatives? To learn more about these important questions, NOS Jeugdjournaal (national TV news bulletin for children) came to the UMCG animal facility to have a look. ERIBA scientist Judith Paridaen explained her work with Zebrafish.

See pages 41–43 for more details.



Facts and Figures



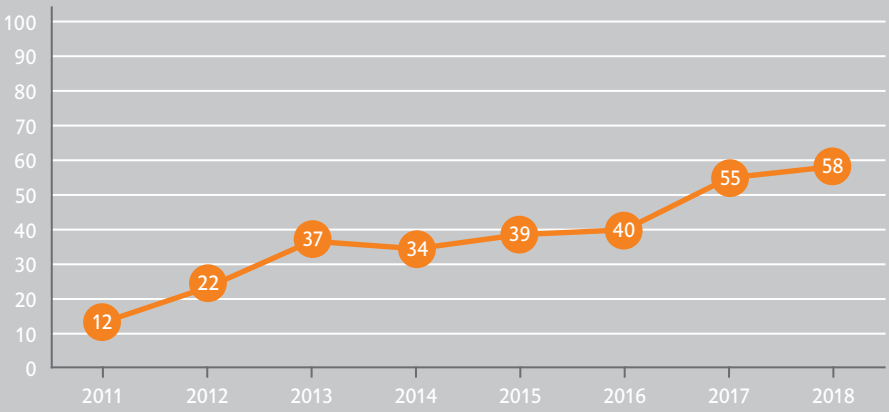
Scientific Publications

2018

58*

* Out of 58 papers 6 are preprints deposited in bioRxiv.

NUMBER OF SCIENTIFIC PUBLICATIONS FROM 2011 ONWARDS



Publications per Research Group

Laboratory of Gene Regulation in Ageing and Age-related Diseases

Group Leader: Cor Calkhoven

1. Sahm A, Bens M, Szafranski, K, Holtze S, Groth M, Görlach M, **Calkhoven CF**, Müller C, Schwab M, Kestler HA, Cellerino A, Burda H, Hildebrandt T, Dammann P and Platzer M Long-lived rodents reveal signatures of positive selection in genes associated with lifespan. PLoS Genet. 2018 Mar 23;14(3):e1007272

2. Müller C, Zidek LM, Ackermann T, de Jong T, Liu P, Kliche V, Zaini MA, Kortman G, Harkema L, Verbeek DS, Tuckermann JP, von Maltzahn J, de Bruin A, Guryev V, Wang ZQ, **Calkhoven CF**. Reduced expression of C/EBPβ-LIP extends health- and lifespan in mice. Elife. 2018 Jun 4;7. pii: e34985

3. Hartleben G, Müller C, Krämer A, Schimmel H, Zidek LM, Dornblut C, Winkler R, Eichwald S, Kortman G, Kosan C, Kluiver J, Petersen I, van den Berg A, Wang Z-Q, **Calkhoven. CF**. Tuberous sclerosis complex is required for tumor maintenance in MYC-driven Burkitt's lymphoma. EMBO J. 2018 Nov 2;37(21).

4. Zaini MA, Müller C, de Jong TV, Ackermann T, Hartleben G, Kortman G, Gührs KH, Fusetti F, Krämer OH, **Guryev V**, **Calkhoven CF**. A p300 and SIRT1 Regulated Acetylation Switch of C/EBPα Controls Mitochondrial Function. Cell Rep. 2018 Jan 9;22(2): 497-511.

Laboratory of Molecular Neurobiology of Ageing

Group Leader: Ellen Nollen

1. Javer A, Currie M, Lee CW, Hokanson J, Li K, Martineau CN, Yemini E, Grundy LJ, Li C, Ch'ng Q, Schafer WR, **Nollen EAA**, Kerr R, Brown AEX. An open-source platform for analyzing and sharing worm-behavior data. Nat Methods. 2018 Sep;15(9):645-646.

2. Perni M, Flagmeier P, Limbocker R, Cascella R, Aprile FA, Galvagnion C, Heller GT, Meisl G, Chen SW, Kumita JR, Challa PK, Kirkegaard JB, Cohen SIA, Mannini B, Barbut D, **Nollen EAA**, Cecchi C, Cremades N, Knowles TPJ, Chiti F, Zasloff M, Vendruscolo M, Dobson CM. Multistep Inhibition of α-Synuclein Aggregation and Toxicity in Vitro and in Vivo by Trodusquemine. ACS Chem Biol. 2018 Aug 17;13(8):2308-2319.

3. Perni M, Challa PK, Kirkegaard JB, Limbocker R, Koopman M, Hardenberg MC, Sormanni P, Müller T, Saar KL, Roode LWY, Habchi J, Vecchi G, Fernando N, Casford S, **Nollen EAA**, Vendruscolo M, Dobson CM, Knowles TPJ. Massively parallel C. elegans tracking provides multi-dimensional fingerprints for phenotypic discovery. J Neurosci Methods. 2018 Aug 1;306:57-67.

4. Sin, O., Mata-Cabana, A., Seinstra, R. I. and **Nollen EAA** Filter Retardation Assay for Detecting and Quantifying Polyglutamine Aggregates Using Caenorhabditis elegans Lysates. Bio-protocol 2018 8(19): e3042.

5. Mata-Cabana, A., Sin, O., Seinstra, R. I. and **Nollen EAA** Nuclear/Cytoplasmic Fractionation of Proteins from Caenorhabditis elegans. Bio-protocol 2018 8(20): e3053.

6. Perni M, Casford S, Aprile FA, **Nollen EAA**, Knowles TPJ, Vendruscolo M, Dobson CM. J Vis Automated Behavioral Analysis of Large C. elegans Populations Using a Wide Field-of-view Tracking Platform. Exp. 2018 Nov 28;(141).

Laboratory of Stem cell regulation and mechanisms of regeneration

Group Leader: Eugene Berezikov

1. Grudniewska M, Mouton S, Grelling M, Wolters AHG, Kuipers J, Giepmans BNG, **Berezikov E** A novel flatworm-specific gene implicated in reproduction in Macrostomum lignano. Scientific Reports. 16-02-2018

2. Mouton S, Grudniewska M, Glazenburg L., **Guryev V**, **Berezikov E**. Resilience to aging in the regeneration-capable flatworm Macrostomum lignano. Aging Cell 2018; e12739

3. Mouton S, Wudarski J, Grudniewska M and **Berezikov E** The regenerative flatworm Macrostomum lignano, a model organism with high experimental potential. Int. J. Dev. Biol. 62: 551 - 558 (2018).

4. Lengerer B, Wunderer J, Pjeta R, Carta G, Kao D, Aboobaker A, Beisel C, **Berezikov E**, Salvenmoser W, Ladurner P. Organ specific gene expression in the regenerating tail of Macrostomum lignano. Dev Biol. 2018 Jan 15;433(2):448-460.

5. Ovchinnikova E, Hoes M, Ustyantsev K, Bomer N, de Jong TV, van der Mei H, **Berezikov E**, van der Meer P Modeling Human Cardiac Hypertrophy in Stem Cell-Derived Cardiomyocytes. Stem Cell Reports. 2018 Mar 13;10(3):794-807.

6. Kenny NJ, de Goeij JM, de Bakker DM, Whalen CG, **Berezikov E**, Riesgo A. Mar Genomics. Towards the identification of ancestrally shared regenerative mechanisms across the Metazoa: A Transcriptomic case study in the Demosponge Halisarca caerulea. 2018 Feb;37:135-147.

7. Ebbing A, Vértesy Á, Betist MC, Spanjaard B, Junker JP, **Berezikov E**, van Oudenaarden A, Korswagen HC. Spatial Transcriptomics of C. elegans Males and Hermaphrodites Identifies Sex-Specific Differences in Gene Expression Patterns. Dev Cell. 2018 Dec 17;47(6):801-813

Laboratory of Genomic Instability in Development and Disease

Group Leader: Floris Foijer

1. van Gijn SE, Wierenga E, van den Tempel N, Kok YP, Heijink AM, **Spierings DCJ**, **Foijer F**, van Vugt MATM, Fehrmann RSN. TPX2/Aurora kinase A signaling as a potential therapeutic target in genomically unstable cancer cells. Oncogene. 2019; 38(6): 852-867; Epub 2018 Sep 3.

2. Macedo JC, Vaz S, Bakker B, Ribeiro R, Bakker PL, Escandell JM, Ferreira MG, Medema R, **Foijer F**, Logarinho E. FoxM1 repression during human aging leads to mitotic decline and aneuploidy-driven full senescence. Nat Commun. 2018 Jul 19;9(1):2834.

3. Worrall JT, Tamura N, Mazzagatti A, Shaikh N, van Lingen T, Bakker B, **Spierings DCJ**, Vladimirou E, **Foijer F**, McClelland SE. Non-random Mis-segregation of Human Chromosomes. Cell Rep. 2018 Jun 12;23(11):3366-3380.

4. Zomerman WW, Plasschaert SLA, Conroy S, Scherpen FJ, Meeuwsen-de Boer TGJ, Lourens HJ, Guerrero Llobet S, Smit MJ, Slagter-Menkema L, Seitz A, Gidding CEM, Hulleman E, Wesseling P, Meijer L, van Kempen LC, van den Berg A, Warmerdam DO, Kruyt FAE, **Foijer F**, van Vugt MATM, den Dunnen WFA, Hoving EW, **Guryev V**, de Bont ESJM, Bruggeman SWM. Identification of Two Protein-Signaling States Delineating Transcriptionally Heterogeneous Human Medulloblastoma. Cell Rep. 2018 Mar 20;22(12):3206-3216.

5. Schukken KM, **Foijer F**. Bioessays. CIN and Aneuploidy: Different Concepts, Different Consequences. 2018 Jan;40(1). doi: 10.1002/bies.201700147.

6. van den Bos H, Bakker B, **Spierings DCJ**, **Lansdorp PM**, **Foijer F**. Single-cell sequencing to quantify genomic integrity in cancer. Int J Biochem Cell Biol. 2018 Jan;94:146-150.

7. Benedict B van Harn T, Dekker M, Hermsen S, Kucukosmanoglu A, Pieters W, Delzenne-Goette E, Dorsman J, Petermann E, **Foijer F**, te Riele H. Loss of p53 suppresses replication-stress-induced DNA breakage in G1/S checkpoint deficient cells. Elife. 2018 Oct 16;7. pii: e37868

8. Simões-Sousa S, Littler, S, Thompson S, Minshall P, Whaley H, Bakker B, Belkot K, Moralli D, Graham H, Bronder D, Tighe A, **Spierings, DCJ**, Bah N, Green C, **Foijer F**, Townsend P, and Taylor SS. The p38 alpha stress kinase suppresses aneuploidy tolerance by limiting the Warburg effect. Cell Rep. 2018 Oct 16;25(3):749-760

9. van den Bos H, Bakker B, Taudt A, **Guryev V**, **Colomé-Tatché M**, **Lansdorp PM**, **Foijer F** and **Spierings DCJ**. Quantification of aneuploidy in mammalian systems. Methods Mol Biol. 2019;1896:159-190

10. Wielders CLC, van Nierop P, Vormer TL, **Foijer F**, Verheij J, Lodder JC, Andersen JB, Mansvelder HD, Te Riele H. RNAi screening of subtracted transcriptomes reveals tumor suppression by taurine-activated GABAA receptors involved in volume regulation. PLoS One. 2018 May 22;13(5):e0196979.

11. **Preprint:** *Bakker B, Terra J, Zhou L, Racz E, Paljic S, Garcia-Martinez J, Oliveira V, Bakker PL,* **Spierings DCJ**, *Jonkman MF,* **Foijer F**. *Single cell DNA sequencing reveals distincs molecular types of basal cell carcinoma with unique transcriptome features. bioRxiv, 492199; doi: https://doi.org/10.1101/492199, December 11, 2018.*

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

1. Han Y, Eipel M, Franzen J, Sakk V, Dethmers-Ausema B, Yndriago L, Izeta A, **de Haan G**, Geiger H, Wagner W. Epigenetic age-predictor for mice based on three CpG sites. Elife. 2018 Aug 24;7. pii: e37462.

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

1. Tavano S, Taverna E, Kalebic N, Haffner C, Namba T, Dahl A, Wilsch-Bräuninger M, **Paridaen JTML**, Huttner WB. Insm1 Induces Neural Progenitor Delamination in Developing Neocortex via Downregulation of the Adherens Junction Belt-Specific Protein Plekha7. Neuron. 2018 Mar 21;97(6):1299-1314.

2. **Preprint:** *Kostic M,* **Paridaen JTML**, *Long K, Kalebic N, Langen B, Wimberger P, Kawasaki H, Namba T, Huttner WB. YAP activity is necessary and sufficient for basal progenitor abundance and proliferation in the developing neocortex. bioRxiv, 416537, September 23, 2018.*

Laboratory of Cellular Biochemistry
Group Leader: Liesbeth Veenhoff

1. Liu B, Mavrova SN, van den Berg J, Kristensen SK, Mantovanelli L, **Veenhoff LM**, Poolman B, Boersma AJ. Influence of Fluorescent Protein Maturation on FRET Measurements in Living Cells. ACS Sens. 2018 Sep 28;3(9):1735-1742.

2. **Preprint:** *Novarina D, Janssens G, Bokern K, Schut T, van Oerle N, Kazemier HG,* **Veenhoff LM** *&* **Chang M** *(2018). A genome-wide screen identifies genes that suppress the accumulation of spontaneous mutations in young and aged yeast cells. bioRxiv. DOI: 10.1101/492587*

3. Irina L Rempel, Matthew M Crane, Ankur Mishra, Daniel PMJansen, Georges Janssens, Petra Popken, Matt Kaeberlein, Erik van der Giessen, Patrick Onck, Anton Steen, **Veenhoff LM** Age-dependent deterioration of nuclear pore assembly in mitotic cells decreases transport dynamics bioRxiv 477802; doi: https://doi.org/10.1101/477802

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

1. Kohli J, Campisi J, **Demaria M** A novel suicide gene therapy for the treatment of p16Ink4a-overexpressing tumors. Oncotarget. 2017 Dec 28;9(7):7274-7281

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Laboratory of Telomeres and Genome Integrity
Group Leader: Michael Chang

1. van Mourik PM, de Jong J, Sharma S, Kav ek A, Chabes A and **Chang M** Upregulation of dNTP Levels After Telomerase Inactivation Influences Telomerase-Independent Telomere Maintenance Pathway Choice in Saccharomyces cerevisiae. G3. 2018 Jul 31;8(8):2551-2558

2. Carmona-Gutierrez D, Bauer MA, Zimmermann A, Aguilera A, Austriaco N, Ayscough K, Balzan R, Bar-Nun S, Barrientos A, Belenky P, Blondel M, Braun RJ, Breitenbach M, Burhans WC, Büttner S, Cavalieri D, **Chang M**, Cooper KF, Côrte-Real M, Costa V, Cullin C, Dawes I, Dengjel J, Dickman MB, Eisenberg T, Fahrenkrog B, Fasel N, Fröhlich KU, Gargouri L, Giannattasio S, Goffrini P, Gourlay CW, Grant CM, Greenwood MT, Guaragnella N, Heger T, Heinisch J, Herker E, Herrmann JM, Hofer S, Jiménez-Ruiz A, Jungwirth H, Kainz K, Kontoyiannis DP, Ludovico P, Manon S, Martegani E, Mazzoni C, Megeney LA, Meisinger C, Nielsen J, Nyström T, Osiewacz HD, Outeiro TF, Park HO, Pendl T, Petranovic D, Picot S, Polcˇic P, Powers T, Ramsdale M, Rinnerthaler M, Rockenfeller P, Ruckenstuhl C, Schaffrath R, Segovia M, Severin FF, Sharon A, Sigrist SJ, Sommer-Ruck C, Sousa MJ, Johan M. Thevelein JM, Thevissen K, Titorenko V, Toledano MB, Tuite M, Vögtle FN, Westermann B, Winderickx J, Wissing S, Wölfl S, Zhang ZJ, Zhao RY, Zhou B, Galluzzi L, Kroemer G, Madeo F Guidelines and recommendations on yeast cell death nomenclature. Microb Cell. 2018 Jan 1;5(1):4-31

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Laboratory of Genetic Instability and Ageing
Group Leader: Peter Lansdorp

1. van Wietmarschen N , Merzouk S, Halsema N, **Spierings DCJ**, **Guryev V**, **Lansdorp PM** BLM helicase suppresses recombination at G-quadruplex motifs in transcribed genes. Nat Commun. 2018 Jan 18;9(1):271.

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3. Worrall JT, Tamura N, Mazzagatti A, Shaikh N, van Lingen T, Bakker B, **Spierings DCJ**, Vladimirou E, **Foijer F**, McClelland SE. Non-random Mis-segregation of Human Chromosomes. Cell Rep. 2018 Jun 12;23(11):3366-3380.

4. van Gijn SE, Wierenga E, van den Tempel N, Kok YP, Heijink AM, **Spierings DCJ**, **Foijer F**, van Vugt MATM, Fehrmann RSN. TPX2/Aurora kinase A signaling as a potential therapeutic target in genomically unstable cancer cells. Oncogene. 2019; 38(6):852-867 ; Epub 2018 Sep 3.

5. van den Bos H, Bakker B, Taudt A, **Guryev V**, **Colomé-Tatché M**, **Lansdorp PM**, **Foijer F** and **Spierings DCJ**. Quantification of aneuploidy in mammalian systems. Methods Mol Biol. 2019;1896:159-190

6. **Preprint:** *Bakker B, Terra J, Zhou L, Racz E, Paljic S, Garcia-Martinez J, Oliveira V, Bakker PL,* **Spierings DCJ**, *Jonkman MF,* **Foijer F**. *Single cell DNA sequencing reveals distincs molecular types of basal cell carcinoma with unique transcriptome features. bioRxiv, 492199; doi: https://doi.org/10.1101/492199, December 11, 2018.*

Laboratory of Genome Structure Ageing
Group Leader: Victor Guryev

1. Mouton S, Grudniewska M, Glazenburg L, **Guryev V**, **Berezikov E**. Resilience to aging in the regeneration-capable flatworm Macrostomum lignano. Aging Cell. 2018 Jun;17(3):e12739.

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5. Müller C, Zidek LM , Ackermann T1, de Jong T1, Liu P3, Kliche V2, Zaini MA1, Kortman G1, Harkema L4, Verbeek DS5, Tuckermann JP3, von Maltzahn J2, de Bruin A4,5, **Guryev V**1, Wang ZQ2, **Calkhoven CF**1,2. Reduced expression of C/EBPβ-LIP extends health and lifespan in mice. Elife. 2018 Jun 4;7. pii: e34985.

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8. Kampen KR, Scherpen FJG, Mahmud H, Ter Elst A, Mulder AB, **Guryev V**, Verhagen HJMP, De Keersmaecker K, Smit L, Kornblau SM, De Bont ES. VEGFC antibody therapy drives differentiation of AML. Cancer Res. 2018 Sep 5. pii: canres.0250.2018.

9. Lauss K, Wardenaar R, Oka R, van Hulten MHA, **Guryev V**, Keurentjes JJB, Stam M, Johannes F. Parental DNA Methylation States Are Associated with Heterosis in Epigenetic Hybrids. 10. Plant Physiol. 2018 Feb;176(2):1627-1645.

10. Zaini MA, Müller C, de Jong TV, Ackermann T, Hartleben G, Kortman G, Gührs KH, Fusetti F, Krämer OH, **Guryev V**, **Calkhoven CF**. A p300 and SIRT1 Regulated Acetylation Switch of C/EBPα Controls Mitochondrial Function. Cell Rep. 2018 Jan 9;22(2):497-511.

11. **Preprint:** *Mark Hills, Ester Falconer, Kieran O'Neil, Ashley Sanders, Kerstin Howe,* **Victor Guryev**, **Peter M Lansdorp** *Construction of whole genomes from scaffolds using single cell Strand-Seq data. doi: https://doi.org/10.1101/271510*

12. **Preprint:** Mark J.P. Chaisson, Ashley D. Sanders, Xuefang Zhao, Ankit Malhotra, David Porubsky, Tobias Rausch, Eugene J. Gardner, Oscar Rodriguez, Li Guo, Ryan L. Collins, Xian Fan, Jia Wen, Robert E. Handsaker, Susan Fairley, Zev N. Kronenberg, Xiangmeng Kong, Fereydoun Hormozdiari, Dillon Lee, Aaron M. Wenger, Alex Hastie, Danny Antaki, Peter Audano, Harrison Brand, Stuart Cantsilieris, Han Cao, Eliza Cerveira, Chong Chen, Xintong Chen, Chen-Shan Chin, Zechen Chong, Nelson T. Chuang, Christine C. Lambert, Deanna M. Church, Laura Clarke, Andrew Farrell, Joey Flores, Timur Galeev, David Gorkin, Madhusudan Gujral, **Victor Guryev**, William Haynes Heaton, Jonas Korlach, Sushant Kumar, Jee Young Kwon, Jong Eun Lee, Joyce Lee, Wan-Ping Lee, Sau Peng Lee, Shantao Li, Patrick Marks, Karine Viaud-Martinez, Sascha Meiers, Katherine M. Munson, Fabio Navarro, Bradley J. Nelson, Conor Nodzak, Amina Noor, Sofia Kyriazopoulou-Panagiotopoulou, Andy Pang, Yunjiang Qiu, Gabriel Rosanio, Mallory Ryan, Adrian Stutz, **Diana C.J. Spierings**, Alistair Ward, AnneMarie E. Welch, Ming Xiao, Wei Xu, Chengsheng Zhang, Qihui Zhu, Xiangqun Zheng-Bradley, Ernesto Lowy, Sergei Yakneen, Steven McCarroll, Goo Jun, Li Ding, Chong Lek Koh, Bing Ren, Paul Flicek, Ken Chen, Mark B. Gerstein, Pui-Yan Kwok, **Peter M. Lansdorp**, Gabor Marth, Jonathan Sebat, Xinghua Shi, Ali Bashir, Kai Ye, Scott E. Devine, Michael Talkowski, Ryan E. Mills, Tobias Marschall, Jan O. Korbel, Evan E. Eichler, Charles Lee Multi-platform discovery of haplotype-resolved structural variation in human genomes doi: https://doi.org/10.1101/193144

Funding/Grants

Funding (Awarded Grants)

2018

€ 3,3 M

2011/2012 · **€ 19,2 M**
2013 · **€ 1,41 M**
2014 · **€ 0,64 M**
2015 · **€ 1,83 M**
2016 · **€ 4,5 M**
2017 · **€ 3,1 M**

Research proposals awarded in 2018

Principal Investigator	Role	Grant	Title	Budget
Cor Calkhoven / Hidde Zuidhof	Applicant	UMCG/KRF	Identifying C/EBPβ-LIP regulators in triple-negative breast cancer	€ 2.616
Diana Spierings / Floris Foijer	Applicant	UMCG/KRF	Towards protocols to make single cell sequencing cheaper	€ 35.000
Ellen Nollen	Applicant	Ubbo Emmius Fund	For research into Alzheimer's disease	€ 17.000
	Applicant	Ubbo Emmius Fund	For research on age-related diseases, in particular Alzheimer's disease	€ 46.000
	Co-applicant	Marie Curie ITN	HealthAge- Joint training an dresearch program on lifespan regulation mechanisms in health and disease	€ 265.620
	Applicant	NWO Aspasia	—	€ 200.000
Floris Foijer	Co-applicant	Abel Tasman PhD fellowship	Developing 3D skin models of basal cell carcinoma	€ 11.000
	Co-applicant	China Scholarship Council (CSC)	In vivo validation of aneuploidy-targeting drugs	€ 210.000
	Co-applicant	Colciencias	Epigenetic dose compensation in aneuploid cells	€ 210.000
	Applicant	KWF	KWF Karyotype evolution and cellular fitness in T-cell lymphoma	€ 691.088
	Co-applicant	de Cock	Optimizing cellular fate mapping of aneuploid cancer cells using live-cell microscopy	€ 4.000

Principal Investigator	Role	Grant	Title	Budget
Floris Foijer	Applicant	Max Planck Institute for Molecular Physiology	Collaboration Transgenic mouse model for GTSE 1	€ 40.000
	Co-applicant	Abel Tasman PhD fellowship	Mutant FUS as a driver of ALS	€ 11.000
Gerald de Haan	Applicant	Tekke Huizinga	3DA treatment as a possible enhancer of hematopoietic stem cell function	€ 10.000
	Co-applicant	Marie Curie ITN	ARCH: age-related changes in hematopoiesis	€ 265.619
Liesbeth Veenhoff	Co-applicant	Rijksuniversiteit Groningen	Bad wiring or bad luck- identifying weak spots in cell's vulnerability to stress	€ 106.223
	Applicant	Ubbo Emmius Fund	Nuclear transport in ageing mitotic cells	€ 19.000
Marco Demaria	Applicant	Cleara Biotech/ Sponsored Research Agreement	Unraveling heterogeneity of senescent cells	€ 723.000
	Applicant	de Cock	Caloriebeperking om de toxiciteit van door chemotherapie geïnduceerde senescentie te verminderen	€ 4.000
Jaskaren Kohli	Applicant	H2020 MSCA-IF	Killing Senescent Cells as a Novel Method to Eliminate Nevi (KILNEV)	€ 165.599
Victor Guryev	Applicant	NWO ALW Open Programma 2018	Functional characterization of Non-reference segments in human genomes	€ 287.038

H2020 MSCA-IF – Horizon 2020, Marie Sk odowska-Curie Actions-Individual Fellowship
KWF – Dutch Cancer Society
NWO – Netherlands Organisation for Scientific Research
De Cock – Jan Kornelis de Cock Foundation
UMCG/KRF – University Medical Center Groningen/ Cancer Research Funds

Invited Speakers

In 2018, many eminent scientists have been invited to give talks and lectures in ERIBA and University Medical Center Groningen.

Speakers	Title of talk/Lecture	Date	Invited by	Meeting
Marc Vermulst	Transcription errors;a novel link between DNA Damage, aging and Alzheimer disease	11 January 2018	Michael Chang	Molecular Medicine Series
Martin Reijns	Linking DNA damage and innate immunity,relevant to autoinflammatory disease and cancer	25 January 2018	Floris Foijer	Molecular Medicine Series
Bill Keyes	Investigating cellular senescence in development, cancer and regeneration	15 February 2018	Marco Demaria	Molecular Medicine Series
Helder Maiato	Chromosome-intrinsic and -extrinsic factors involved in mitotic fidelity	8 March 2018	Floris Foijer	Molecular Medicine Series
Helen Morrison	Inflammaging - Age related decline of the peripheral nervous system	15 March 2018	Cor Calkhoven	Molecular Medicine Series
Natascia Ventura	C. elegans as a powerful model organism to assess the role of mitochondria in the aging process'	11 June 2018	Gerald de Haan	PI candidate
Tessa Sinnige	Towards a molecular understanding of protein aggregation in vivo'.	11 June 2018	Gerald de Haan	PI candidate
John Lacava	Affinity proteomics as fishing LINE: human retrotransposons and other whale tales.'	12 June 2018	Gerald de Haan	PI candidate
Mark Hipp	'Proteostasis impairment in protein misfolding and aggregation diseases.	12 June 2018	Gerald de Haan	PI candidate
James Stewart	Mitochondrial DNA Mutations and Mitochondrial Dysfunction in Mouse Models of Ageing and Disease.'	18 June 2018	Gerald de Haan	PI candidate
David Vichez	'Proteostasis of aging and stem cells'.	18 June 2018	Gerald de Haan	PI candidate
Miguel Coelho	Experimental evolution of genetic instability: implications for cancer and aging"	25 June 2018	Gerald de Haan	PI candidate
Alessandro Prigione	Mitochondria in fate reprogramming and neurodegeneration	25 June 2018	Gerald de Haan	PI candidate
Alexander van Oudenaarden	Whole-organism clone-tracing using -cell sequencing	5 July 2018	Gerald de Haan	Molecular Medicine Series
Andrew Holland	Once and only once: Molecular mechanisms underlying the control of centrosome copy number and their dysregulation in disease	14 July 2018	Floris Foijer	Molecular Medicine Series
Dawn Lin	steady-state and emergency dendritic cell development at the single cell level	31 August 2018	Gerald de Haan	Friday afternoon meeting ERIBA
Hein te Riele	Studying Lynch syndrome - without a break	12 September 2018	Floris Foijer	Minisymposium genomic instability
Sarah McClelland	'Focus on the Individual; The importance of chromosome-specific biology in generating aneuploidy patterns in cancer.	12 September 2019	Floris Foijer	Minisymposium genomic instability

Speakers	Title of talk/Lecture	Date	Invited by	Meeting
Vincenzo Sorrentino	Autophagy, danger, death and immunity in cancer therapy	25 September 2018	Marco Demaria	Molecular Medicine Series
Linda Clijsters	how E2F transcription factors are regulated, and how this regulation is important in maintaining cellular fitness	3 October 2018	Floris Foijer/ Marcel van Vugt	Special seminar
Catherine Rabouille	Cell biology of stress: Cytoplasmic rearrangements and signaling events	5 October 2018	Liesbeth Veenhoff	Friday afternoon meeting ERIBA
Lorenzo Galluzi	Autophagy,dancer,death and immunity in cancer therapy	11 October 2018	Marco Demaria	Molecular Medicine Series
Rene Bernards	A one two punch model for cancer therapy	16 October 2018	Marco Demaria	Special seminar
Jurgen Marteijn	'Transcription Coupled Repair, when transcription meets DNA damage'	18 October 2018	Floris Foijer	Special seminar
Gerben Vader	Molecular machines in control of meiotic Chromosome breakage and repair	18 October 2018	Floris Foijer	Molecular Medicine Series
Jeroen Pasterkamp	Dissecting the molecular mechanisms of neurological disease	1 November 2018	Ellen Nollen	Molecular Medicine Series
Marcel van Vugt	Consequences of defective DNA repair	2 November 2018	Floris Foijer	Friday afternoon meeting ERIBA.
Alex Bird	Tuning microtubule instability to ensure genome stability: clathrin's role in mitosis	9 November 2018	Floris Foijer	Friday afternoon meeting ERIBA
Francois Paris	Acute and chronic endothelial responses modulated radiation therapy efficacy	15 November 2018	Rob Coppes/ Marco Demaria	Molecular Medicine Series
Vincent Geli	Role of the nuclear pore complex in the repair of damaged telomeres.	3 December 2018	Michael Chang	Promotion Sonia Stinus
David Gisselsson Nord	Evolutionary trajectories of childhood cancer over time and space	6 December 2018	Floris Foijer	Molecular Medicine Series
Elzo de Wit	Functional dissection of the 3D genome	7 December 2018	Floris Foijer/ Diana Spierings	Friday afternoon meeting ERIBA.
John Rossen	Long-read sequencing in the clinical microlab	7 December 2018	Floris Foijer/ Diana Spierings	UMCG Sequencing Technology Symposium
Monique vd Wijst	Personalized co-expression analysis reveals genetic risk factors changing the regulatory wiring of cells	7 December 2018	Floris Foijer/ Diana Spierings	UMCG Sequencing Technology Symposium

People

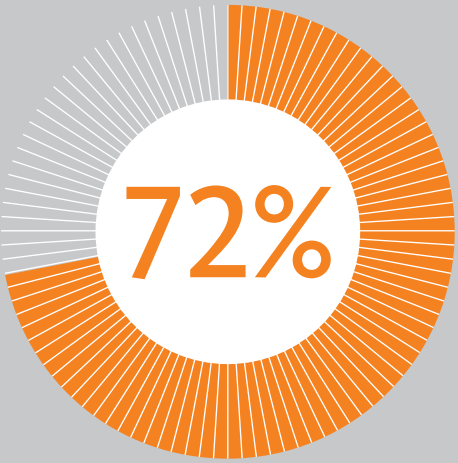
EMPLOYEES

2018

2013 · **81** 2014 · **89** 2015 · **89**
2016 · **92** 2017 · **107**

STAFF UNDER 40 (%)

2018



2013 · **69%** 2014 · **63%** 2015 · **63%**
2016 · **61%** 2017 · **76%**

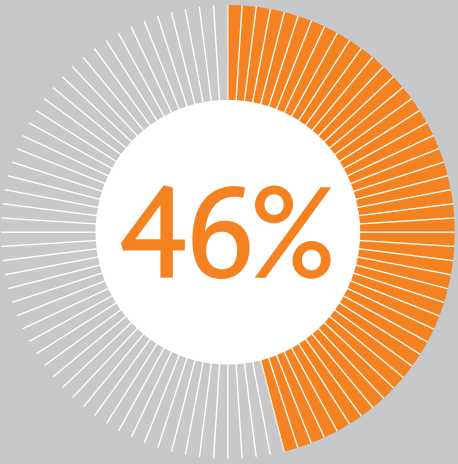
FEMALE EMPLOYEES (%)

2018

2013 · **60%** 2014 · **56%** 2015 · **56%**
2016 · **55%** 2017 · **54%**

INTERNATIONALS (%)

2018



2013 · **47%** 2014 · **48%** 2015 · **47%**
2016 · **45%** 2017 · **49%**

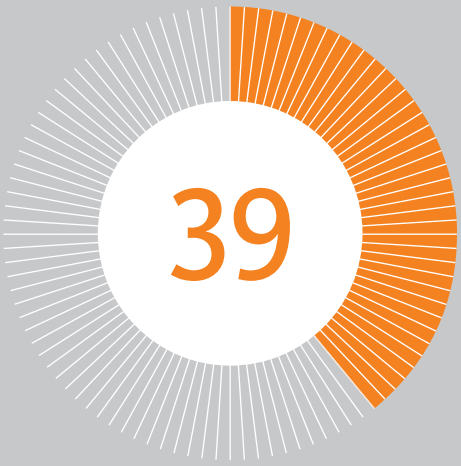
NUMBER OF NATIONALITIES

2018

2013 · **18** 2014 · **17** 2015 · **17**
2016 · **22** 2017 · **23**

PhD STUDENTS HOSTED BY ERIBA (1)

2018

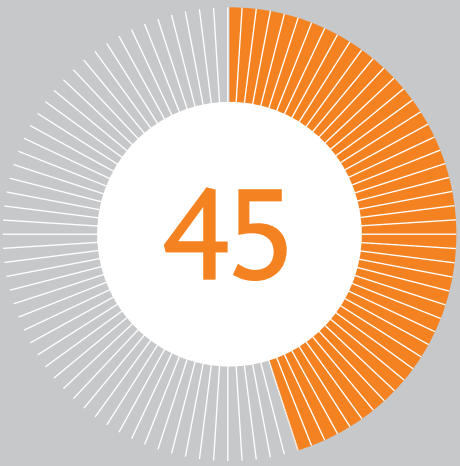


2013 · **22** 2014 · **22** 2015 · **26**
2016 · **27** 2017 · **44**

[1] 10 of these students hosted by ERIBA under the GSMS Bursary Scheme

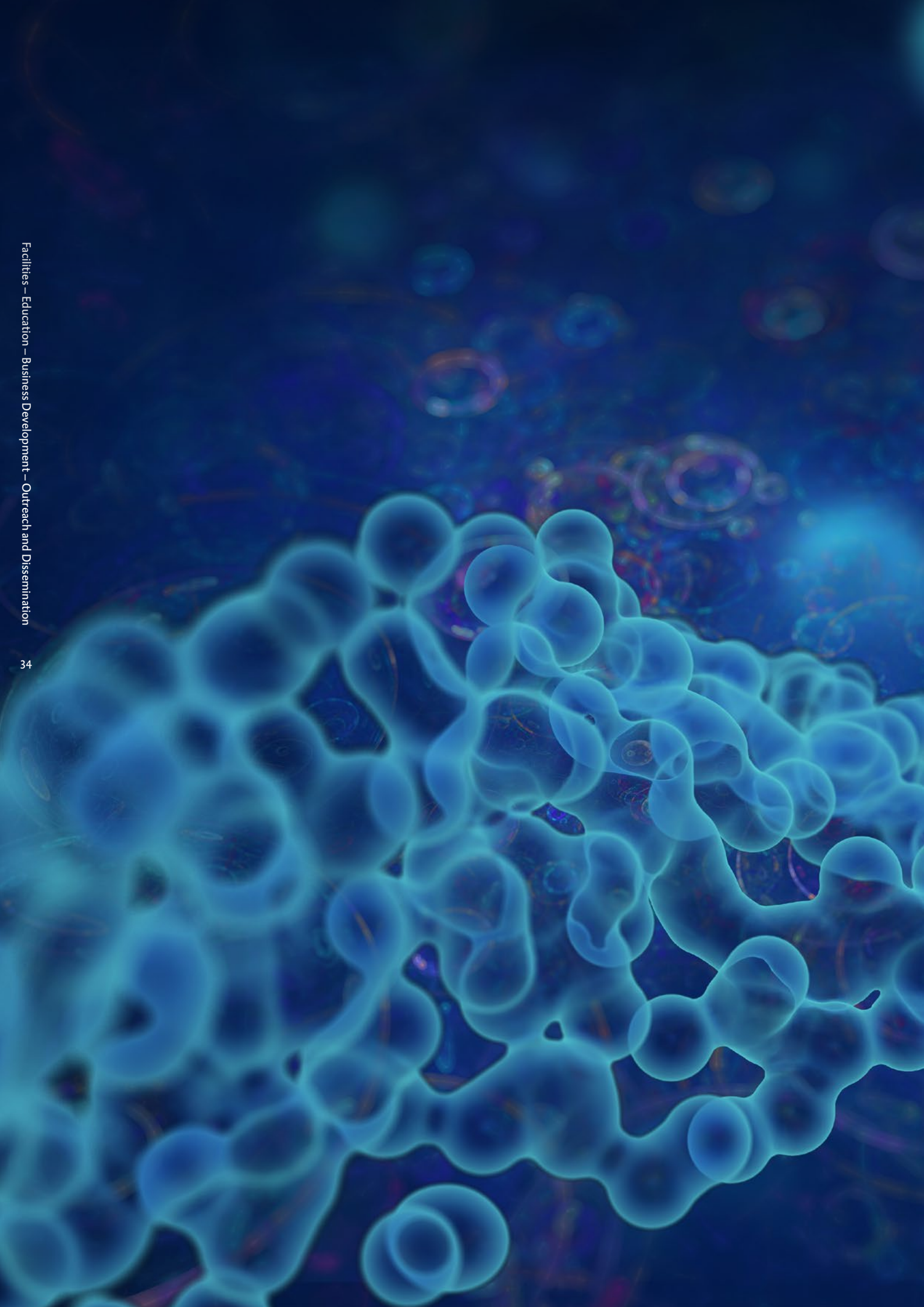
INTERNS (2)

2018



2013 · **17** 2014 · **41** 2015 · **41**
2016 · **26** 2017 · **49**

[2] Students who made internships in various labs



Facilities

Education

Business Development

Outreach and Dissemination

Facilities

iPSC/CRISPR centre

The discovery of protocols to reprogram somatic cells into induced pluripotent stem cells (iPSCs) is revolutionising regenerative medicine. The therapeutic promise of iPSC technology includes the production of isogenic cell lineages and (in the future) tissues to replace body parts that can be autografted in patients when organs are failing. Importantly, when combined with CRISPR genome engineering technology, iPSC technology can be used to cure (mono) genetic diseases, by repairing the disease-causing mutation in patient-derived iPSCs and by differentiating the repaired cells into functional tissues and transplanting them back into the patient. The iPSC/CRISPR centre at ERIBA aims to contribute to this therapeutic promise. For this, we help UMCG and RUG employees with deriving iPSCs and establishing differentiated cultures from these iPSCs. Furthermore, we help our customers with CRISPR genome engineering, including making knockout cell lines, engineering point mutations, tagging endogenous genes, etc. in various cell lines, including iPSCs. Furthermore, we facilitate genome-wide CRISPR functional screens and we engineer mouse models using CRISPR technology. Since the start of the centre in 2014, we accommodated ~100 different projects, and in 2018 we initiated ~30 new projects that include iPSC projects, and CRISPR genome engineering projects in cells and in mice. We implemented a number of differentiation protocols and protocols to grow cerebral organoids and validated the reagents for genome-wide CRISPR screens. Importantly, we trained several PhD students in deriving and maintaining iPSCs and in differentiating iPSCs into various cell types. Furthermore, we hosted MSc students for internships and we organised the CRISPR genome engineering course for Biomedical Sciences MSc students. Finally, we hosted a number of high school students to help them with their biology projects. Next year, we expect to accommodate several new large-scale projects, as we appointed two new postdocs as of Jan 2018, and we will likely invest in infrastructure to automate iPSC culture, thus drastically increasing our capacity for iPSC lines.

Who

Floris Foijer – Coordinator IPSC/CRISPR facility
Bart van de Sluis – Coordinator CRISPR mice
Arun Thiruvalluvan – Postdoctoral Fellow
Dr. René Wardenaar – Postdoctoral Fellow
Sahil Gupta – Postdoctoral Fellow
Jonathan Seiler – Postdocoral Fellow
Mathilde Broekhuis – Technician
Eslie Huizinga – Technician

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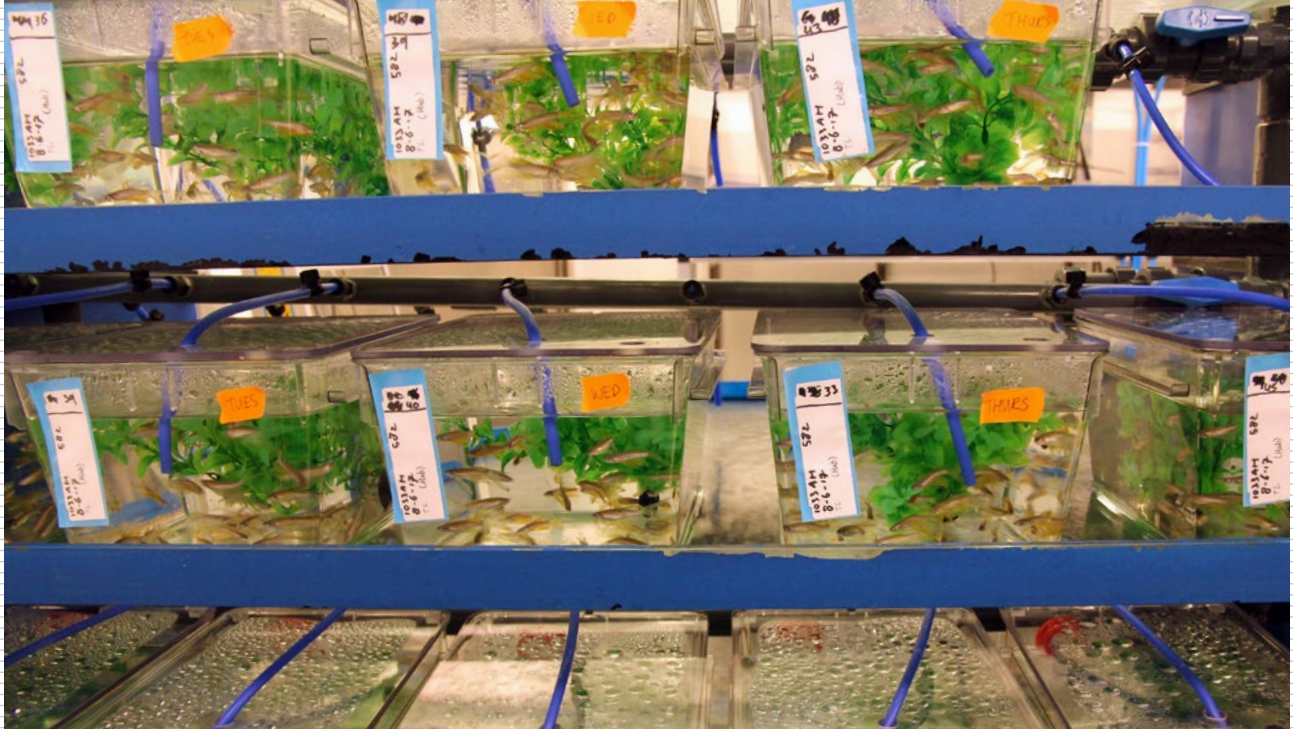

Fish facility

The Central Animal Facility (CDP) in the University Medical Center Groningen is one of the 13 academic experimental animal institutions in the Netherlands. The CDP is a facility where experimental animals are housed, and where animal experimentation is conducted. The CDP supports and facilitates research and education projects involving vertebrate experimental animals, such as rodents and fish.
In 2016, a fish facility was established within the CDP, where state-of-the-art housing is supplied for two species of small fish: killifish (Nothobranchius furzeri), and zebrafish (Danio rerio). Killifish are the shortest living vertebrate experimental animal system, which makes it very suitable for studying ageing processes. They were introduced by the Berezikov lab in the ERIBA as a new model organism to study the biology of ageing in the ERIBA and UMCG. Currently, the CDP is the only facility in the Netherlands that houses killifish. Zebrafish are a very versatile vertebrate experimental animal system that is used extensively in biomedical research, and constitute a cheaper and easy-to-work-with an alternative to rodents.

Key expertise and services

– Dedicated animal care-takers trained in breeding, rearing of fish larvae, general care and health services in small fish species
– Dedicated microinjection and epifluorescence stereomicroscopy setups for visual inspection, analysis, manipulation and microinjection of zebrafish and killifish embryos
– Dedicated incubators for housing fish embryos
– Availability of several strains of wild-type fish, such as AB, TL and Casper (transparent) zebrafish
– Breeding services to obtain embryos of wild-type, and if required, other strains
– Support and advice regarding genomic modification methods, such as transgenesis and CRISPR/cas9-mediated genomic modifications
– Training of new users in fish experimentation (next to obligatory course on Laboratory Animal Science)
– Breeding and care taking, biotechnical support, micro-surgical support, imaging support and animal welfare monitoring

Who

Eugene Berezikov – ERIBA PI (killifish expert)
Joscha Muck – Postdoctoral fellow, ERIBA (killifish expert)
Judith Paridaen – ERIBA PI (zebrafish expert)
Nynke Oosterhof – postdoctoral felow, ERIBA (zebrafish expert)
Alex Kluppel – Manager CDP
Catriene Thuring – Animal Welfare Officer, Deputy Head CDP

Contact

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Education

ERIBA scientists are involved in multiple education activities. The list below is a selection of major contributions to teaching. It excludes a large number of individual lectures and undergraduate student internships.

"Molecular and Genetic Age Research at ERIBA"
10 ECTS, 17 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.

"Editing, regulating and targeting genomes with CRISPR-Cas9"
5 ECTS, 26 MSc biomedical students
Coordinator: **Floris Foijer**
Objectives: A high level of involvement, initiative and creativity is being expected from the participating students. The theoretical basis and the application of gene editing through CRISPR-Cas9 will be taught in a series of 12 lectures followed by practical assignments and laboratory training. CRISPR-Cas9 provides biomedical research with a cut-and-paste toolbox for genome editing in mammalian cells, allowing scientist to cure genetic diseases by repairing the disease causing mutation. The technology is rapidly changing biomedical science and is expected to form the basis of personalized medicine in the future.

"Model organisms in Ageing Research"
3 ECTS 11 BSc medical students (Junior Scientific Master course)
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 lab, altogether giving them an impression of the 'live of a basic biologist'.

"Genome Data for Beginners"
1.5 ECTS, 30 PhD students (GSMS course)
Course coordinator: **Leonid Bystrykh**
Objectives: Online genome databases are rapidly expanding and are central to biological and medical research. Such massive amount of information needs basic understanding of how to find the data of interest and what to do with those data. In this course students practice with data retrieval from GEO, UCSC, Encode, ENSEMBL and other web sites. Basic introduction to RNAseq, ChIPseq, as well as to genomic (promoter) motifs and gene ontology tools is provided. Students are introduced to basic programming in Python, R and several other script types.

Molecular Biology of Ageing and Age related Disease"

5 ECTS, 30 MSc biomedical students

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 is supported by a team of specialists in different fields of ageing who 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 unit is compulsory for the ageing track and is an elective in the other tracks of the programs.

"Current Themes in Healthy Ageing"

5 ECTS, 33 MSc biomedical students

Coordinators: **Marco Demaria** and **Judith Paridaen**

Objectives: Learn leading edge ageing research and interact with prominent aging scientists by following scientific seminars. Biomedical Science students attend 7- scientific seminars and verbally report on content, scientific excellence and track records of the presenters. This course has been growing rapidly and now has > 30 students/year.

"Genomics Biology"

1,5 ECTS, Course for biomed student at Karolinska Institute

Coordinators: **Victor Guryev** and **Leonid Bystrykh**

Victor Guryev and Leonid Bystrykh organized a 1 week Genome Biology course for biomedical students at the Karolinska Institute in Stockholm, Sweden.

Business Development

In 2018 ERIBA launched a biotech start-up company Cleara Biotech B.V. (Cleara), together with collaborators in University Medical Center Utrecht (UMCU) and Medical University of Graz. Cleara is a Netherlands-based biopharmaceutical company that aims to discover and develop new therapeutics targeting senescent cells to treat age-related pathologies and therapy-resistant cancer.

Cleara is working to translate discoveries surrounding the unique properties of senescent cells. This work is being led within Cleara by Marco Demaria of ERIBA, who created genetic tools for identifying senescent cells and also discovered shared mechanisms and genes at the core of the senescence program. Peter de Keizer at the UMCU is leading work on a novel method to remove senescent cells.
Cleara was founded and financed by Apollo Ventures, a life sciences venture capital firm and company builder working across Europe and North America.

CLEARA

Outreach and Dissemination

ERIBA has been consistently engaged in various communication and outreach activities as a mean to effectively bring the general public closer to research. Through public events, activities for schools, tours and many more initiatives, ERIBA seeks to connect a wide range of audiences outside the academia: public in general, secondary education students, industry, decision-makers, media, and patient organisations. Some of our most notable activities in 2018 are listed below.

Media

Judith Paridaen featured on the NOS Jeugdjournaal (national TV news bulletin for children). NOS Jeugdjournaal journalists visited the animal facility to understand the importance and necessity of animal models for research purposes. Judith Paridaen shared and highlighted her research, and explained the importance of animals in research. She showed the zebrafish housing facility, and demonstrated the tools and techniques being used in zebrafish research.
jeugdjournaal.nl/artikel/2228761-waarom-zijn-er-nog-steeds-dierproeven.html
Staff Member Involved: **Judith Paridaen**

Events

Career Day

14th March 2018

Organisers: **Alejandra Hernández Segura, Britt Sterken, Nina Kool, Helena Rico** and **Judith Paridaen**

This exciting event focused on career opportunities outside academia, and featured speakers who discussed how they transitioned from a PhD/postdoc position in academic research to their current position outside academia. ERIBA hosted Elena Herrero Gomez (Syncom), Karin Klauke (Novartis), Louise Stone (Nature Journal), Sylvia Boj (Hubrecht Organoid Technology), Fabrizia Fusetti (QPS), Tim Vos (NWO), Marianna Bevova (University of Liege), Huup Dassen (Freelance Science Journalist). The speakers described their unique backgrounds and provided advice to young researchers looking to pursue careers beyond the academic path. This event was a huge success and motivated us to organise the Career day event again in 2019.

Zpannend Zernike

6th October, 2018

Staff members involved: **Anton Steen**

Volunteers: **Jenny Jaques, Gloria Casas Gimeno, Leen Janssen, Inge Kazemier, Marije Semmelink, Judith Paridaen, Sylvia Hoks**

To create public awareness and inspire scientists of tomorrow every year ERIBA opens its doors to the public as part of the national event Weekend van de Wetenschap. This event is locally known as Zpannend Zernike, in which research institutes, the University of Groningen, the UMCG, and the Hanze Hogeschool team up in Groningen as a single organization. The main focus of Weekend van de Wetenschap/Zpannend Zernike was on activities for primary school children and their families. On Saturday, the 6th of October, 2018 approximately 700 people visited the ERIBA premises. The activities included isolation of DNA, exploring model organisms used for scientific research, a pipetting course, a quiz on organ transplantation, a scientific escape room, and a session on advantages and disadvantages of microbial organisms and their role in society.

Activity

Science in a Box

Staff member involved: **Stijn Mouton**

With the support of ERIBA's Outreach Committee, Dr. Stijn Mouton is currently developing "Science in a Box", a concept linking Scientific Research, Scientific Outreach, and Education. The Science Kits will provide everything needed to perform a biological experiment in the classroom. This unique hands-on experience will help to explore topics such as regeneration, stem cells, and the use of model organisms in scientific research. Moreover, this active approach is an effective classroom method as it encourages student curiosity and can trigger interest in a future scientific career.

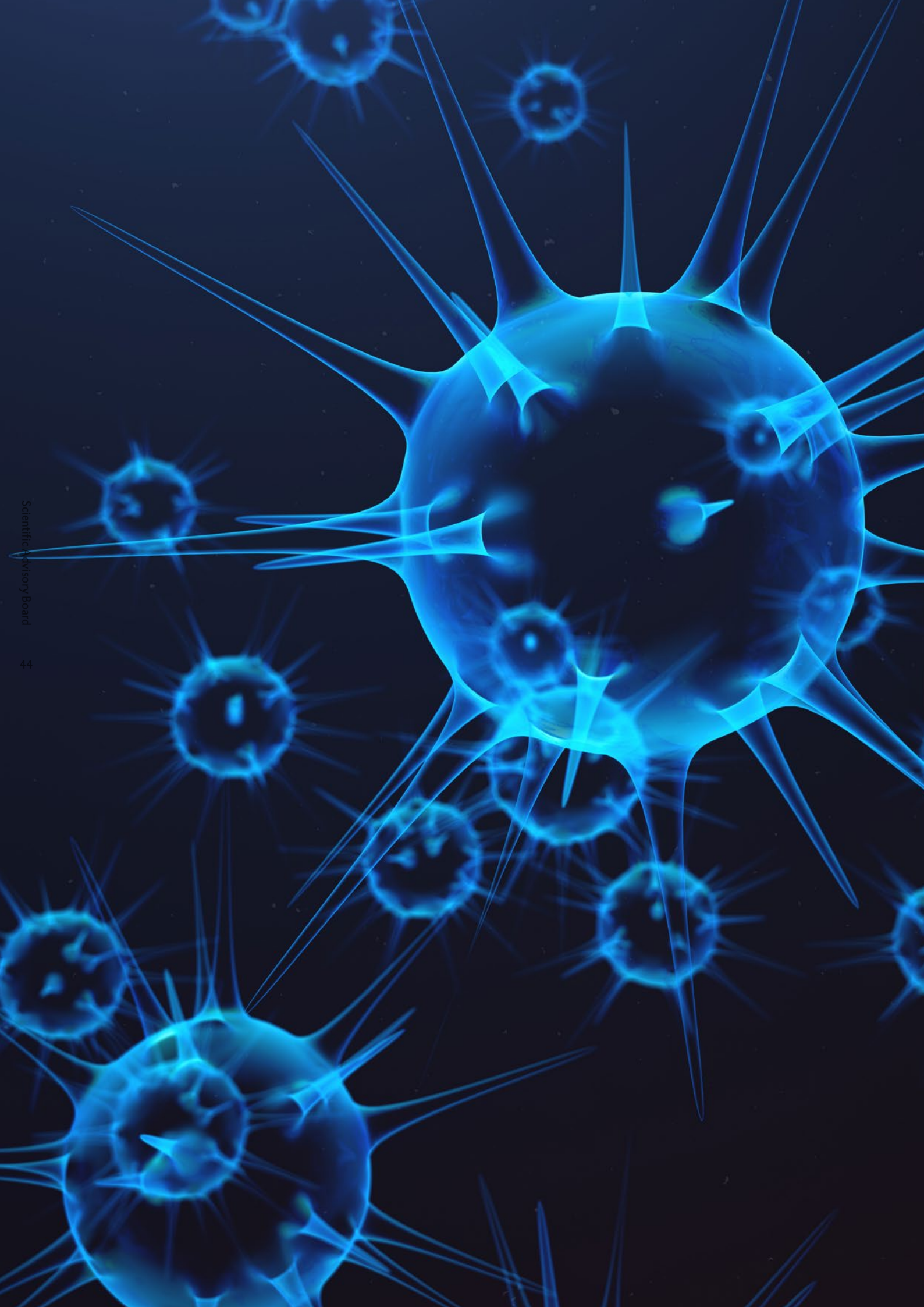
After a year of development, "Science in a Box" will be launched in 2019, and will initially offer two Science Kits:

– The "Planaria Regeneration Box" contains worms of the flatworm species **Schmidtea mediterranea**, all required materials, and an illustrated protocol for conducting a pre-designed regeneration experiment;
– The "Planaria Culture Box" contains worms and materials to maintain a culture of **Schmidtea mediterranea**, and enables to personally design and perform a scientific project.

In the future, we hope to develop additional Science Kits, using multiple models and covering different scientific areas. The aim is to create a large, long-term ERIBA Outreach project, which brings students, teachers, and scientists together in an interactive network.

Visits from International Delegations

In 2018, ERIBA hosted and welcomed many distinguished visitors. These included ambassador to the USA Mr. Pete Hoekstra (who happened to be born 200 meters from ERIBA), Ambassador to India Mr. Venu Rajamony, and Ambassador to Germany Mr. Dirk Brengelmann. A delegation from the Chinese University of Hong Kong (CUHK) visited ERIBA to discuss career planning and development, identify and foster future collaborations with ERIBA.



Scientific Advisory Board

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

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

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

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The Pediatric Oncology Foundation Groningen (SKOG)

SKOG
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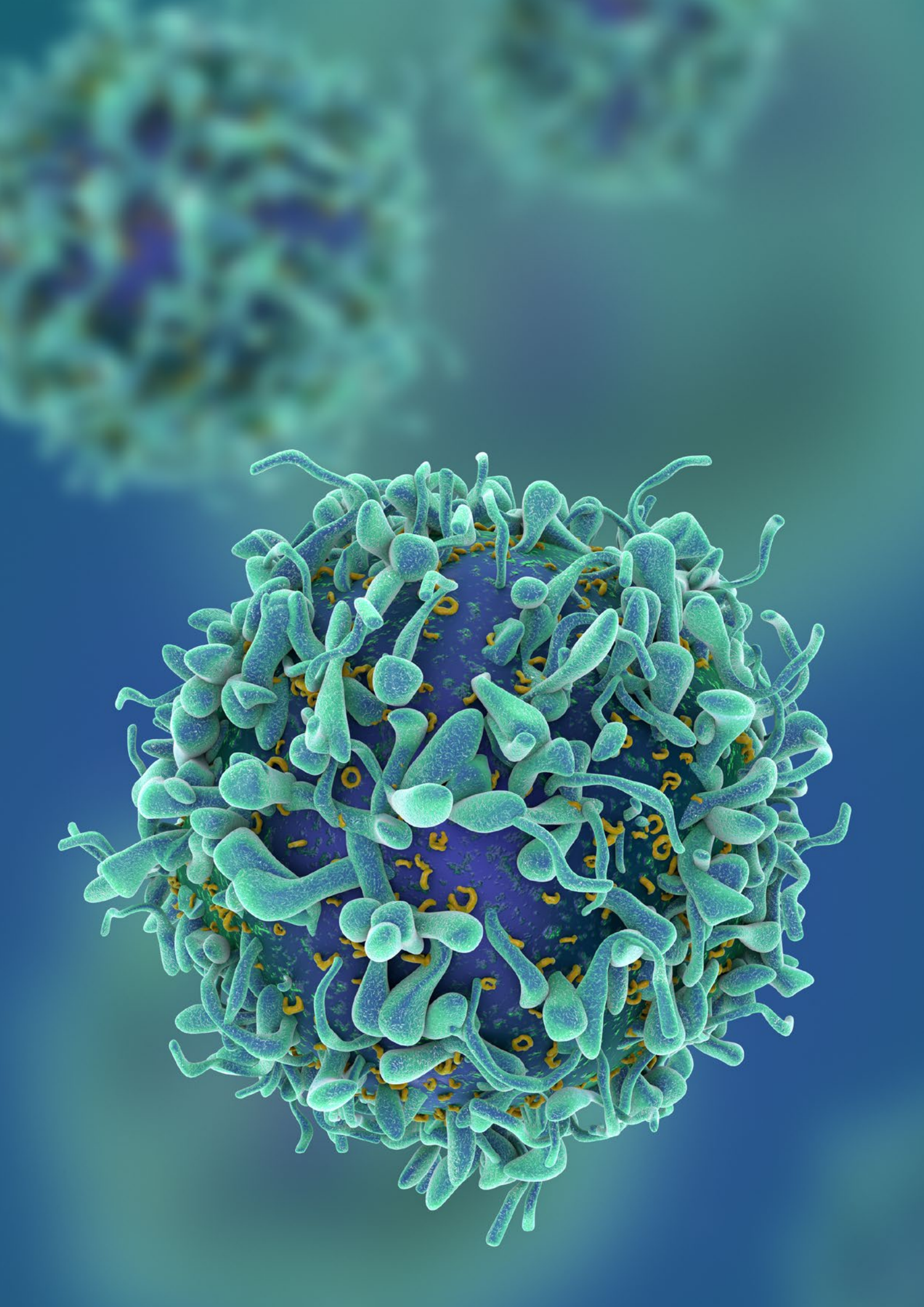

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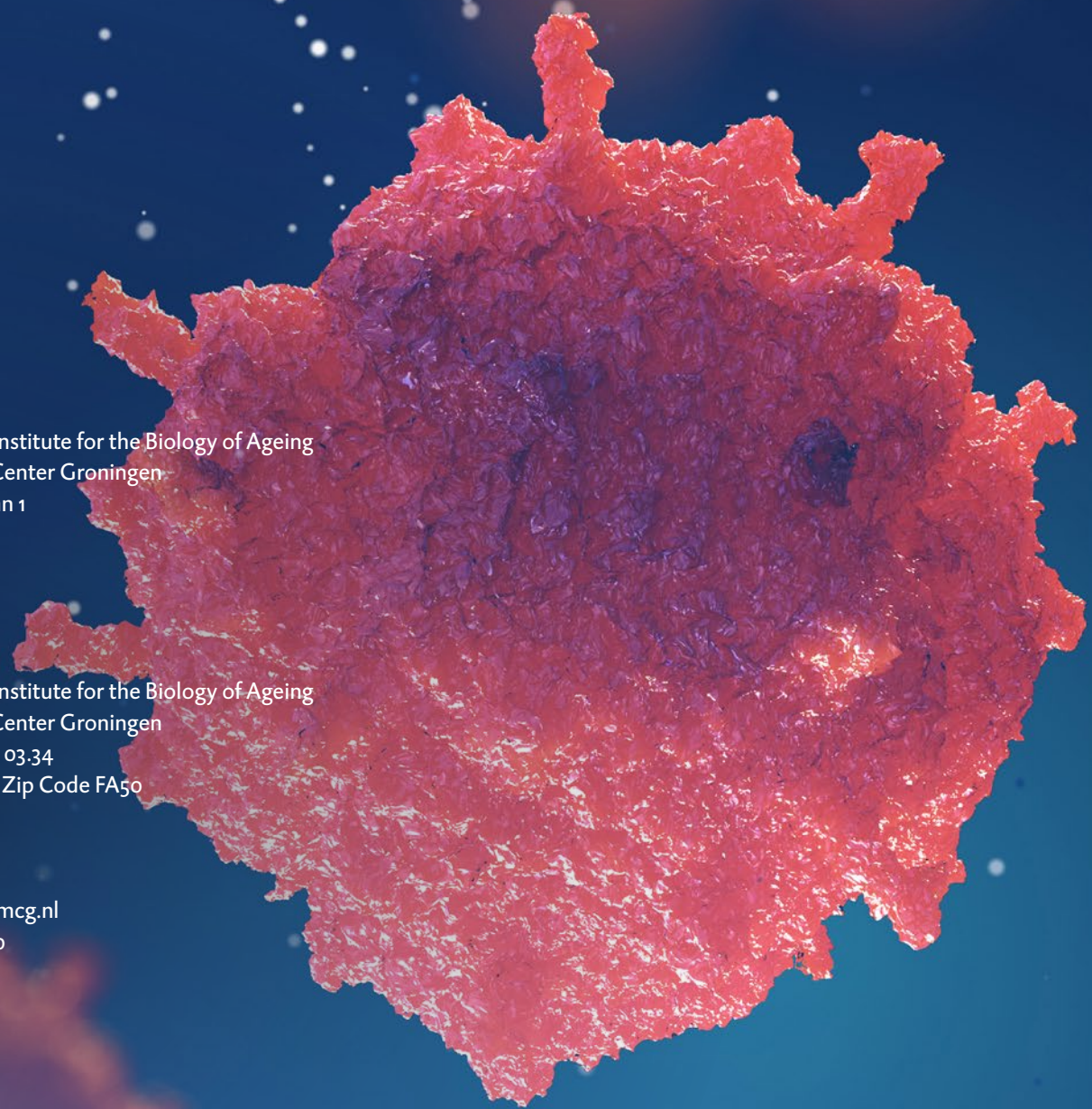

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