ERIBA

European Research Institute for the Biology of Ageing

Annual Report 2019

2019

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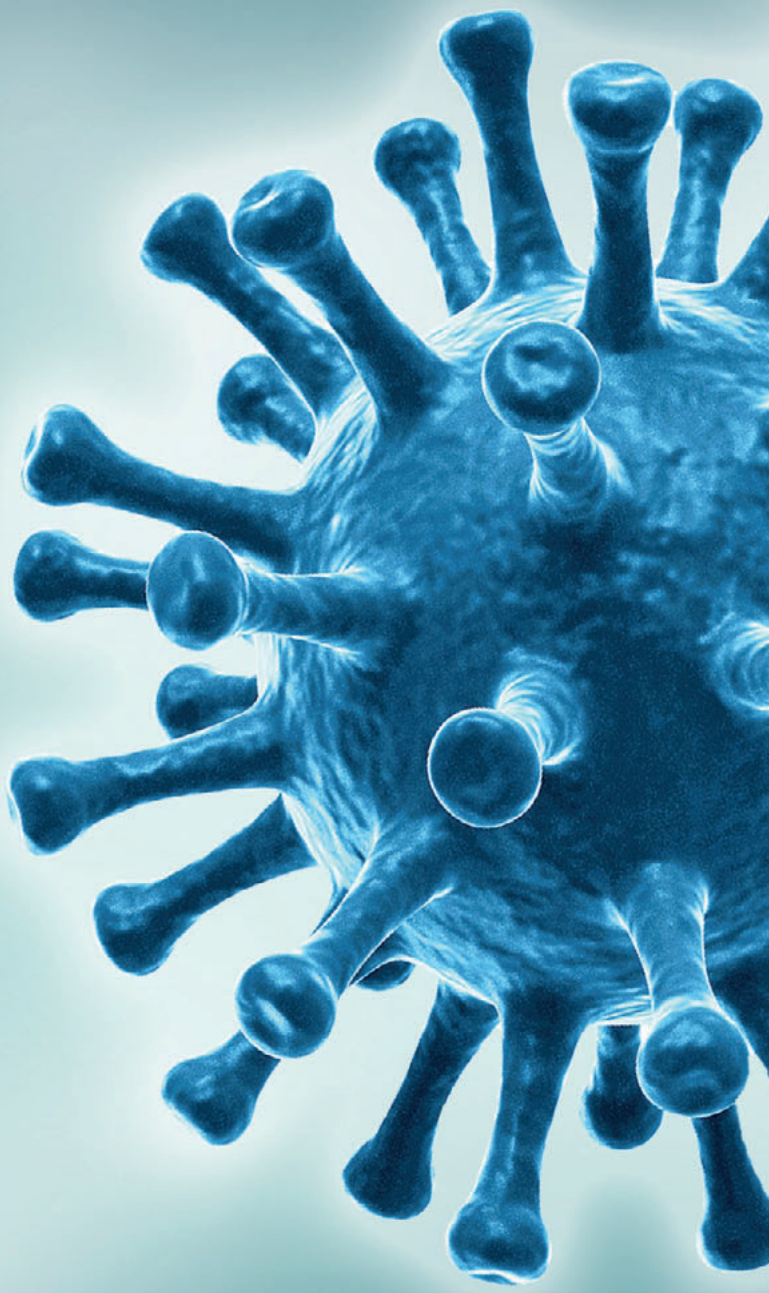
Annual Report
2019

2019

Welcome to our Annual Report 2019



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Printing:
Ridderprint BV | Anand Baldew

Copies:
100

Annual Report
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Foreword by the Director

2019 in review

Gerald de Haan
Scientific Director

It is a great pleasure to present to you the 2019 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 2019.

I write these words in the midst of the Covid-19 pandemic. This pandemic may very well have a major effect on global research and education for quite some time to come. One aspect, highly relevant to what we do in ERIBA, relates to how the virus differentially affects individuals in society. For as yet unclear reasons, globally elderly individuals are far more susceptible to develop critical morbidity compared to young. Thus, like many other diseases such as cancer and dementia, Covid-19 is very much an age-associated disease.

In ERIBA we study what ageing is, and why elderly individuals become frail and susceptible to disease. It is our firm believe that only if we understand why cells and tissues in our body gradually cease proper functioning as we age will it be possible to intervene in the ageing process. Therefore, if anything, the Covid-19 pandemic has reinforced our raison d'etre and has made us more committed than ever to contribute to finding out why we age.

In 2019 we published 61 papers, more than any other year. The large majority of these papers were the result of teams of ERIBA scientists collaborating with each other, or with researchers outside our Institute.

''In ERIBA we study what ageing is, and why elderly individuals become frail and susceptible to disease.''

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 remain very committed to contributing to talent development in the field of ageing. In 2019 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.

Progress in science is exponential, and it is of imminent importance to share our findings with society. In 2019 ERIBA scientists were involved in many of such outreach activities. You will find a long list of all our efforts in this Annual Report. We do not only organize these outreach activities because they are fun (which they are!), but also to convey the message that 'finding things out' is essential to offer future therapeutic opportunities to confront age-associated diseases. We need to understand how proteins properly fold in the brain if it is our aim to target Alzheimer disease. We need to understand why the immune system in elderly functions poorly if it is our aim to ensure that a future Covid-20 pandemic has the same disastrous consequences as the -19 pandemic that hit us this year.

In 2019 we recruited John LaCava from Rockefeller University in New York City to ERIBA. John is an expert in proteomics and develops sophisticated technology to capture protein complexes from cells to molecularly dissect functional pathways. We very much welcome John and anticipate that his expertise will result in many collaborative projects with scientists in ERIBA and the UMCG.

In October 2019 we have organized, for the third time, the biennial conference series on the Molecular Biology of Ageing Meeting in Groningen. We assembled a stellar team of international speakers to cover many aspects of the ageing process. One of the keynote speakers was Titia de Lange, who was awarded an honorary doctorate from our University earlier in the year. Little did we know at that time that this was one of the last ageing meeting to be held for quite some time, as the viral pandemic has seriously affected international conferencing. Excitingly, as I write this foreword, many webinars related to ageing have been launched, including a series by Marco Demaria in ERIBA.

The upcoming year, 2020, will be an odd year, which all of us will remember vividly. It is uncertain how much longer Covid-19 will affect the research and education agenda. However, whatever the future will bring, our mission and ambition are more viable and relevant than ever before.

Gerald de Haan

Scientific Director

May 2020

Ageing Research at ERIBA

ERIBA is an internationally recognised European research institute located in the city of Groningen, The Netherlands.

Since its inception in 2009, the institute has grown and established itself as one of the leading research institutes in the field of ageing biology. The institute has state-of-art facilities and focuses on research to understand the causes of ageing.

Research

Research at ERIBA aims to address phenomena such as genome stability, protein homeostasis decline, metabolic decline, and stem cell loss of function. These phenomena have been implicated in various age-related diseases such as cancer, neurodegeneration, and diabetes. The research at ERIBA investigates the molecular and cellular mechanisms underlying ageing and age-related diseases.

New strategies

ERIBA aims to develop new strategies to prevent age-related diseases and increase the healthy life span of individuals. The institute also aims to provide evidence-based recommendations for healthy ageing by discovering new drug targets, specialized disease models, and assays for the purpose of adding more healthy years to human life.

ERIBA is currently the home of 13 research groups that cover a wide range of age-related topics.

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.

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.

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.

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".

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's group.

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.

Macromolecules and Interactomes

The laboratory of John LaCava focuses broadly on characterizing the contributions of dysregulated macromolecular interactions to diseases. To characterize such interactions the group uses combination of biochemical, “omics” and computational approaches.

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.

Gene Regulation In Ageing and Age-Related Diseases

The group of Cor Calkoven is particularly interested in the function of mRNA control elements, protein factors and microRNAs that are involved in mTORC1-controlled processes.

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.

Quantitative Epigenetics

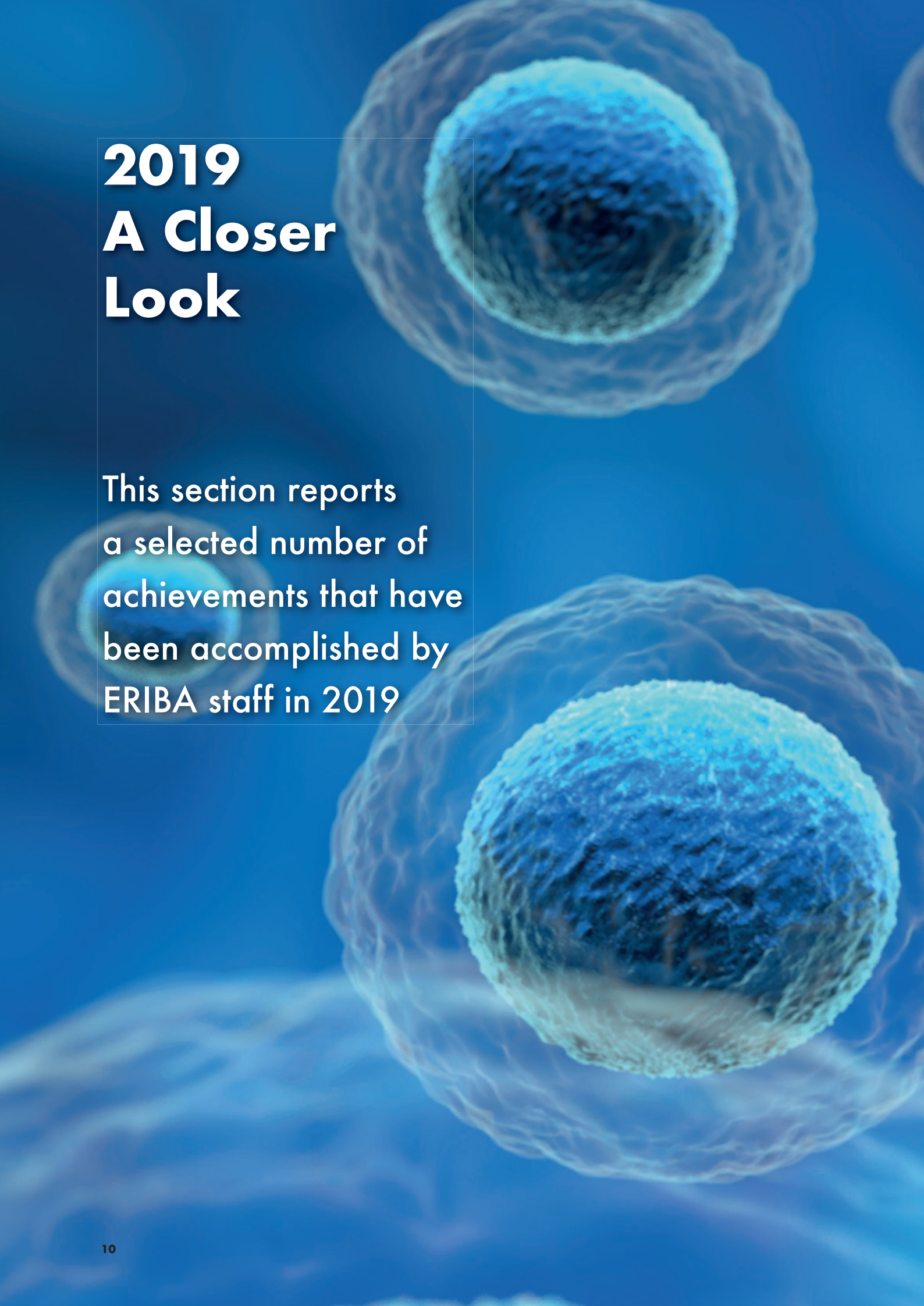
The group of Maria Colomé-Tatché is interested in understanding the epigenetic changes that take place during the processes of development, ageing and disease.

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.

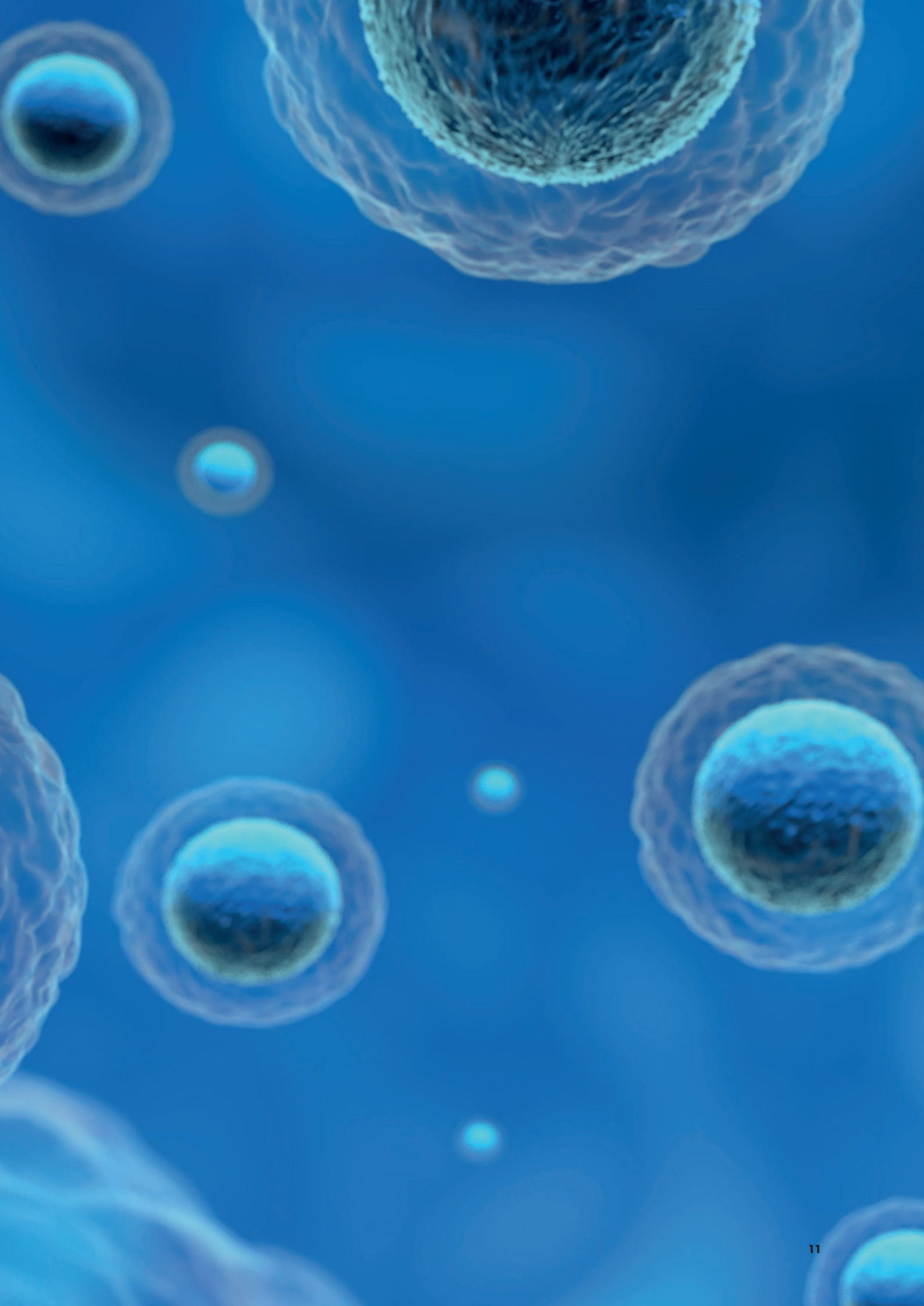
Cellular Biochemistry

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.



2019 A Closer Look

This section reports a selected number of achievements that have been accomplished by ERIBA staff in 2019



Scientific Publications

In 2019, ERIBA scientists published a record number of 61 papers in reputed scientific journals. Many of the published papers were the result of fruitful national and international collaborations employing a multidisciplinary approach. Numerous joint projects were initiated within ERIBA, between scientists in ERIBA and research groups at the University Medical Center Groningen and the Faculty of Science and Engineering of the University of Groningen, and with international partners. A snapshot of ERIBA's team scientific achievements are highlighted below:

Cor Calkhoven's group

In this review the group described the accumulating evidence that CCAAT/enhancer binding protein (C/EBP) transcription factors are determinants of biological age and lifespan. C/EBPβ and C/EBPα are controlled by the lifespan regulator mechanistic/mammalian target of rapamycin complex 1 (mTORC1) and play an important role in energy homeostasis and adipose tissue differentiation. Converging data are discussed, which indicate that aberrant DNA methylation can affect ageing via C/EBPβ. Changes in epigenetic DNA methylation are the most promising predictor of biological age and lifespan in humans, but whether methylation changes affect ageing is unresolved. The group discussed the emerging causal nexus between C/EBPβ, energy metabolism, and DNA demethylation in organismal ageing. In addition, they discussed possible roles of other C/EBP members.

Niehrs, C. and Calkhoven, C.F. (2019) The emerging role of C/EBPβ and epigenetic DNA methylation in ageing. Trends Genet, DOI: 10.1016/j.tig.2019.11.005

Michael Chang's group

Genome mutations are known to accumulate as cells and organisms age, and this has been proposed as a possible causal factor of ageing. What is unclear is whether the rate of spontaneous mutations is constant during ageing, and whether there are pathways that become important to suppress the accumulation of mutations specifically in aged cells. Here, the group developed a high-throughput approach to identify genes affecting low-frequency events in yeast, and used it to find genes that suppress the accumulation of mutations during yeast ageing. They found that in the absence of PEX19, which encodes a protein required for peroxisome function, the spontaneous mutation rate increases in aged cells. This observation provides a novel link between peroxisomes, genome maintenance, and ageing.

Novarina D, Janssens GE, Bokern K, Schut T, van Oerle NC, Kazemier HG, Veenhoff LM, Chang M (2019) A genome-wide screen identifies genes that suppress the accumulation of spontaneous mutations in young and aged yeast cells. Aging Cell. 2020 Feb;19(2):e13084

Floris Foijer's group

Chromosomal instability is a common feature in cancer that leads to cells with an abnormal DNA content, also known as aneuploidy. In addition to aneuploidy, ongoing chromosomal instability also leads to cell-to-cell variation in DNA content between individual cancer cells. This CIN contributes to intratumour heterogeneity and clinical response. In this paper, the group investigated chromosomal instability and the resulting karyotype dynamics in primary human colon cancer organoids using time-lapse imaging and single cell sequencing. They found that these tumor organoids display high grade CIN, even those that are associated with a microsatellite instability (MIN) phenotype, which traditionally is seen as a mutually exclusive feature with CIN tumors. The work showed that ongoing CIN is a common feature of colon cancer that shapes the karyotype landscape of these tumors, thus driving its ongoing evolution.

Bolhaqueiro ACF, Ponsioen B, Bakker B, Klaasen SJ, Kucukkose E, van Jaarsveld RH, Vivié J, Verlaan-Klink I, Hami N, Spierings DCJ, Sasaki N, Dutta D, Boj SF, Vries RGJ, Lansdorp PM, van de Wetering M, van Oudenaarden A, Clevers H, Kranenburg O, Foijer F, Snippert HJG, Kops GJPL (2019) Ongoing chromosomal instability and karyotype evolution in human colorectal cancer organoids. Nat Genet. 2019 May;51(5):824-834. doi: 10.1038/s41588-019-0399-6. Epub 2019 Apr 29.

Gerald de Haan's group

In this study, the group demonstrated that the epigenetic reader protein CBX7 possesses the ability to control self-renewal of human hematopoietic stem and progenitor cells (HSPCs) and does so by repressing genes involved in differentiation, DNA and chromatin maintenance, and cell cycle control. CBX7 is upregulated in acute myeloid leukemia (AML), and showed that its genetic or pharmacological repression in leukemic cells inhibited proliferation and induced differentiation. They revealed several non-histone protein interactions between CBX7 and the H3K9 methyltransferases SETDB1, EHMT1, and EHMT2. These CBX7-binding proteins possess a trimethylated lysine peptide motif highly similar to the canonical CBX7 target H3K27me3. Indeed, depletion of SETDB1 in AML cells phenocopied repression of CBX7. The research identified CBX7 as an important regulator of self-renewal and uncover non-canonical crosstalk between distinct pathways, revealing therapeutic opportunities for leukemia.

Jung J, Buisman SC, Weersing E, Dethmers-Ausema A, Zwart E, Schepers H, Dekker MR, Lazare SS, Hammerl F, Skokova Y, Kooistra SM, Klauke K, Poot RA, Bystrykh LV, de Haan G (2019)CBX7 Induces Self-Renewal of Human Normal and Malignant Hematopoietic Stem and Progenitor Cells by Canonical and Non-canonical Interactions. Cell Rep. 2019 Feb 12;26(7):1906-1918.e8. doi: 10.1016/j.celrep.2019.01.050.

Liesbeth Veenhoff's group

Nuclear Pore Complex (NPC) function in ageing has received much attention in the context of postmitotic (chronologically) ageing cells, such as neurons, and indeed a large body of data now implicate NPC function in neurodegenerative diseases. Veenhoff group studied the fate of NPCs in single dividing yeast cells with the anticipation that the insights may be relevant to ageing of mitotic cells such as stem cells. Overall, their data is consistent with a model where NPC assembly and quality control are compromised in mitotic ageing and where misassembled NPCs accumulate in aged cells.

Rempel IL, Crane MM, Thaller DJ, Mishra A, Jansen DP, Janssens G, Popken P, Akşit A, Kaeberlein M, van der Giessen E, Steen A, Onck PR, Lusk CP, Veenhoff LM.(2019) Age-dependent deterioration of nuclear pore assembly in mitotic cells decreases transport dynamics. Elife. 2019 Jun 3;8. pii: e48186. doi: 10.7554/eLife.48186.

Peter Lansdorp's group

The mapping of structural genomic variants remains an enormous challenge for current sequencing techniques. Long read technologies such as PacBio have the advantage that mapping to a reference genome is not absolutely required. However, such complete "de novo" genome assembly is problematic for large segments of our genome that are flanked by highly repetitive DNA. The latter are easily detected using the single cell Strand-seq technique developed in the Lansdorp lab. In this paper a combination of PacBio and Strand-seq was used to generate a highly accurate map of a human genome.

Vollger MR, Logsdon GA, Audano PA, Sulovari A, Porubsky D, Peluso P, Wenger AM, Concepcion GT, Kronenberg ZN, Munson KM, Baker C, Sanders AD, Spierings DCJ, Lansdorp PM, Surti U, Hunkapiller MW, Eichler EE. (2019) Improved assembly and variant detection of a haploid human genome using single-molecule, high-fidelity long reads. Ann Hum Genet. 2019 Nov. doi.org/10.1111/ahg.12364

Marco Demaria's group

Cellular senescence is a cell state implicated in various physiological processes and a wide spectrum of age-related diseases. Recently, interest in therapeutically targeting senescence to improve healthy ageing and age-related disease (senotherapeutics) has been growing rapidly. Thus, the accurate detection of senescent cells, especially in vivo, is essential. In this review, the group defined and discussed key cellular and molecular features of senescence and provide recommendations on how to use them as biomarkers. Demaria's group also presented a resource tool to facilitate the identification of genes linked with senescence (SeneQuest, available at http://Senequest.net). Lastly, they proposed an algorithm to accurately assess and quantify senescence, both in cultured cells and in vivo.

Gorgoulis V, Adams PD, Alimonti A, Bennett DC, Bischof O, Bishop C, Campisi J, Collado M, Evangelou K, Ferbeyre G, Gil J, Hara E, Krizhanovsky V, Jurk D, Maier AB, Narita M, Niedernhofer L, Passos JF, Robbins PD, Schmitt CA, Sedivy J, Vougas K, von Zglinicki T, Zhou D, Serrano M, Demaria M. (2019) Cellular Senescence: Defining a Path Forward. Cell. 2019 Oct 31;179(4):813-827. doi: 10.1016/j.cell.2019.10.005.

Ellen Nollen's group

This study, led by former ERIBA staff member Christian Riedel, aimed to identify anti-ageing drugs to improve human health- and lifespan. Using machine learning on RNA profiles of age-stratified human tissues, classifiers were found that could distinguish young from old tissues. Application of these age-classifiers to RNA profiles of human cells treated with 1309 different drugs led to the identification of several compounds that induced youthful RNA profiles. Two of these compounds, the heat shock protein 90 (Hsp90) inhibitors monorden and tanespimycin, were selected based on their ability to improve health- and lifespan in the nematode C.elegans. Protection by Hsp90 inhibitors required activation of the unfolded protein response. As Hsp90 inhibitors are known to protect against chronic inflammation and senescence, their improving protein homeostasis as proposed in this study would add yet another mode of geroprotection. Future work in humans will be required to determine their therapeutic potential.

Janssens GE, Lin XX, Millan-Ariño L, Kavšek A, Sen I, Seinstra RI, Stroustrup N, Nollen EAA, Riedel CG (2019) Transcriptomics-Based Screening Identifies Pharmacological Inhibition of Hsp90 as a Means to Defer Ageing. Cell Rep. 2019 Apr 9;27(2):467-480.e6. doi: 10.1016/j.celrep.2019.03.044.

Eugene Berezikov's group

In this work we systematically investigated how different culture temperatures can affect the biology of the regenerating flatworm model organism Macrostomum lignano. We show that altering temperature conditions can be used to reduce the time required to establish M. lignano cultures, perform RNAi experiments, store important lines, and optimize microinjection procedures for transgenesis. These findings will help to optimize the design of experiments in M. lignano, and thus facilitate future research using this model organism.

> Wudarski J, Ustyantsev K, Glazenburg L, Berezikov E (2019) Influence of temperature on development, reproduction and regeneration in the flatworm model organism, Macrostomum lignano. Zoological Lett. 2019 Feb 12;5:7. doi: 10.1186/s40851-019-0122-6. eCollection 2019.

Victor Guryev's group

Affordable sequencing has greatly advanced our understanding of changes in transcription programs and their relation to ageing and diseases. The typical analysis of gene expression data focuses on the finding of genes that show differential expression between patient groups. Unfortunately, in such analysis, variability in gene expression is often ignored as it is treated as a nuisance that only diminishes statistical power. At the same time, gene expression is naturally a stochastic process, and in some cases its fluctuation, rather than the mean RNA copy number, could be significantly influenced by an experimental factor or a physiological state. In this paper Guryev's group discussed approaches to quantification of expression variability, its contribution to understanding of the principles underlying physiological homeostasis, and its potential to uncover additional molecular phenotypes associated with age-related diseases.

> de Jong TV, Moshkin YM, Guryev V (2019) Gene expression variability: the other dimension in transcriptome analysis. Physiol Genomics. 2019 May 1;51(5):145-158. doi: 10.1152/physiolgenomics.00128.2018. Epub 2019 Mar 15.

John LaCava's group

Retrotransposons are 'selfish' DNA sequences that have the ability to replicate themselves in host genomes via a 'copy and paste' mechanism.
The proliferation of LINE-1 retrotransposons is apparent at the genetic level in cancers and cell lines – providing unequivocal evidence for the expression of the enzymatic, replicative component of LINE-1: ORF2p. However, ORF2p continues to elude direct detection. LaCava's group and their collaborators took a deep dive into data from the NCI's Clinical Proteomic Tumor Analysis Consortium in search of ORF2p peptide signatures. Failing to find convincing evidence in the archived data, they raised a collection of monoclonal antibodies against the protein in an effort to bolster capture and detection. Although the antibodies validated excellently against the target in ectopic expression, endogenous ORF2p remained elusive. Finally, they took to affinity isolating endogenous LINE-1 RNPs, via ORF1p, directly from resected patient colorectal cancers – reporting the first endogenous LINE-1 cancer interactome. Although ORF2p was not identified among the co-isolated proteins, they demonstrated the technical feasibility of studying disease-related protein complexes directly in patient tumors and identified overlaps between endogenous LINE-1 colorectal cancer protein interactions and those previously described from ectopic LINE-1 expressing HEK-293T cells. They concluded that more sensitive methods will be needed to robustly detect ORF2p and propose targeted mass spectrometry and proximity ligation immuno-fluorescence as two future directions.

> Ardeljan, D., Wang, X., Oghbaie, M., Taylor, M., Husband, D., Deshpande, V., Steranka, J., Gorbounov, M., Yang, W., Sie, B., Larman, H., Jiang, H., Molloy, K., Altukhov, I., Li, Z., McKerrow, W., Fenyö, D., Burns, K., LaCava, J. (2020). LINE-1 ORF2p expression is nearly imperceptible in human cancers. Mobile DNA 11(1), 1 - 19. https://dx.doi.org/10.1186/s13100-019-0191-2

Grants

In 2019 ERIBA secured €2.77 million from grants. This included prestigious grants from the Dutch Cancer Society, ZonMw, and the ALS foundation. The institute also received a grant to bolster public-private research. Detailed information about ERIBA grants and funding can be found on page 32

Awards

Victor Guryev's team from ERIBA together with a RUG team (RNA TORCH) won the BioHack 2019 award. The team received an award at the bioinformatics hackathon held in Saint Petersburg, Russia. Teams consisting of biologists and programmers participated in the event to solve one of 40 problems within 48 hours.

Glòria Casas Gimeno, PhD student in the Paridaen lab, received a Poster Prize at the HBIGS International Winter School on "Molecular Mechanisms in Mitosis". Glòria presented a poster on her PhD project on the role of cellular centrioles in asymmetric stem cell division. She also received another poster prize in International Conference on cilia, flagella and Centrosomes, Imagine Institute, Paris.

Katya Dvorianinova, PhD student in Paridaen lab received EMBO Travel award to attend EMBO practical course Optogenetics-From Design to Cell Signalling to Tissue Morphogenesis at EMBL Heidelberg, Germany.

Sonja Buisman, PhD student in de Haan's group received Cancer Research Center Groningen (CRCG) prize for best short-pitch.

Sabrina Jacobs, PhD student in de Haan's group received Cancer Research Center Groningen (CRCG) prize for best short-pitch.

Graduations

In 2019, four young scientists graduated from ERIBA as PhD students and since have moved to new positions either in academia or industry:

Alejandra Hernandez Segura (Demaria's lab) is currently at the Rijksinstituut voor Volksgezondheid en Milieu (RIVM), The Netherlands,

Irina Rempel (Veenhoff's lab) is at Novartis, Basel, Switzerland,

Paula van Mourik (Chang's lab) is at EV Biotech, Groningen, The Netherlands,

Tristan de Jong (Guryev's lab) is self-employed.

Scientific Dissemination and Outreach

ERIBA has been actively involved in scientific dissemination and public outreach. The first Career day organised in 2018 was a huge success with contributions from people from both academia and industry. On Wednesday 24 April 2019, the second edition of the ERIBA Career Day took place, where PhD students and Postdocs explored career opportunities outside of academia. More than 60 PhD students and postdocs from ERIBA and the UMCG attended the meeting.

The scientists at ERIBA are committed to many outreach activities and nurturing the young minds to build the scientists of tomorrow. Keeping our commitment to the cause we opened our doors to the public to share scientific knowledge at the Zpannend Zernike event. More than 680 people attended the event and enjoyed the scientific events specifically tailored to them.

To link scientific research, scientific outreach, and education ERIBA's outreach committee member developed "Science in a Box" concept. This concept was designed to trigger student curiosity and to encourage the students towards a scientific career. The idea behind the concept was to have a science experiment, specially designed for school students enclosed in a box.

As part of the Science Fair 'University of Noorderzon' organized by the Young Academy Groningen the ERIBA scientists imparted research knowledge to kids and their parents. To further enhance the outreach, and to explain the importance of animals in research our scientist presented in the summer school Healthy ageing, and ERIBA hosted a visit for high school students to teach them about one of our animal models: Zebrafish. At ERIBA both experienced scientists and young scientists of tomorrow actively participate in outreach events. To this cause, the young scientists at ERIBA represented the institute at "scientific pub crawl", delivering interesting scientific lectures to the general public at one of the largest science festivals (www.pintofscience.nl).

To stimulate new ideas and to foster scientific collaborations in the rapidly growing field of ageing research ERIBA organised the 3rd Molecular Biology of Ageing meeting. This meeting was attended by people from all across the globe and was a huge success.

See page 55 for more details.

Facts and Figures

Looking back to 2019 though facts and figures

Scientific Publications

SCIENTIFIC PUBLICATIONS

2019

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2012 - 22
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2014 - 34
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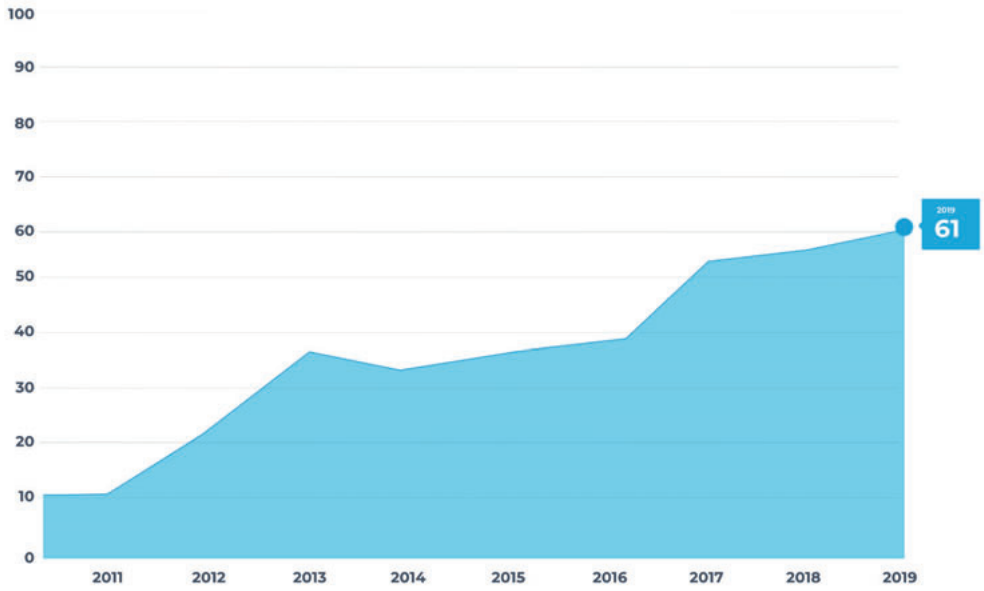

Publications per Research Group

Laboratory of Gene Regulation in Ageing and Age-related Diseases

Group Leader: Cor Calkhoven

1. Ackermann T, Hartleben G, Müller C, Mastrobuoni G, Groth M, Sterken BA, Zaini MA, Youssef SA, Zuidhof HR, Krauss SR, Kortman G, de Haan G, de Bruin A, Wang ZQ Platzer M, Kempa S, Calkhoven CF. (2019) C/EBPβ-LIP induces cancer-type metabolic reprogramming by regulating the let-7/LIN28B circuit in mice. Commun Biol. 2019 Jun 14;2:208. doi: 10.1038/s42003-019-0461-z. eCollection 2019.

2. Niehrs, C. and Calkhoven, C.F. (2019) The emerging role of C/EBPβ and epigenetic DNA methylation in ageing. Trends Genet, DOI: 10.1016/j.tig.2019.11.005

3. Bakula, D., Ablasser, A., Aguzzi, A., Antebi, A., Barzilai, N., Bittner, M-I., Borch Jensen, M., Calkhoven, C.F., Chen, D., de Grey, A.D.N.J., Feige, J.N., Georgievskaya, A., Gladyshev, V.N., Golato, T., Gudkov, A.V., Hoppe, T., Kaeberlein, M., Katajisto, P., Kennedy, B.K., Lal, U., Martin-Villalba, A., Moskalev, A.A., Ozerov, I., Petr, M.A., Reason, Rubinsztein, D.C., Tyshkovskiy, A., Vanhaelen, Q., Zhavoronkov, A., Scheibye-Knudsen, M. (2019) Latest advances in ageing research and drug discovery. Aging, DOI: 10.18632/aging.102487

Laboratory of Molecular Neurobiology of Ageing

Group Leader: Ellen Nollen

1. Sorgdrager FJH, Vermeiren Y, Van Faassen M, van der Ley C, Nollen EAA, Kema IP, De Deyn PP. (2019) Age- and disease-specific changes of the kynurenine pathway in Parkinson's and Alzheimer's disease. J Neurochem. 2019 Dec;151(5):656-668. doi: 10.1111/jnc.14843. Epub 2019 Aug 25.

2. Laine RF, Sinnige T, Ma KY, Haack AJ, Poudel C, Gaida P, Curry N, Perni M, Nollen EAA, Dobson CM, Vendruscolo M, Kaminski Schierle GS, Kaminski CF. (2019) Fast Fluorescence Lifetime Imaging Reveals the Aggregation Processes of iα-Synuclein and Polyglutamine in Aging Caenorhabditis elegans. ACS Chem Biol. 2019 Jul 19;14(7):1628-1636. doi: 10.1021/acschembio.9b00354. Epub 2019 Jun 27.

3. Janssens GE, Lin XX, Millan-Ariño L, Kavšek A, Sen I, Seinstra RI, Stroustrup N, Nollen EAA, Riedel CG (2019) Transcriptomics-Based Screening Identifies Pharmacological Inhibition of Hsp90 as a Means to Defer Aging. Cell Rep. 2019 Apr 9;27(2):467-480.e6. doi: 10.1016/j.celrep.2019.03.044.

4. Koopman M, Seinstra RI, Nollen EAA.(2019) C. elegans as a Model for Synucleinopathies and Other Neurodegenerative Diseases: Tools and Techniques. Methods Mol Biol. 2019;1948:93-112. doi: 10.1007/978-1-4939-9124-2_9.

5. Platten M, Nollen EAA, Röhrig UF, Fallarino F, Opitz CA. (2019) Tryptophan metabolism as a common therapeutic target in cancer, neurodegeneration and beyond. Nat Rev Drug Discov. 2019 May;18(5):379-401. doi: 10.1038/s41573-019-0016-5. Review.

6. Koopman M, Hetz C, Nollen EAA (2019).Saved by the Matrix: UPR Independent Survival under ER Stress. Cell. 2019 Nov 27;179(6):1246-1248 doi:10.1016/j.cell.2019.11.012.

7. Sorgdrager FJH, Naudé PJW, Kema IP, Nollen EA, Deyn PP (2019) Tryptophan Metabolism in Inflammaging: From Biomarker to Therapeutic Target. Front Immunol. Oct 30;10:2565. doi: 10.3389/fimmu.2019.02565. eCollection 2019.

Laboratory of Stem cell regulation and mechanisms of regeneration

Group Leader: Eugene Berezikov

1. Oliveira KMC, Barker JH, Berezikov E, Pindur L, Kynigopoulos S, Eischen-Loges M, Han Z, Bhavsar MB, Henrich D, Leppik L.(2019) Electrical stimulation shifts healing/scarring towards regeneration in a rat limb amputation model. Sci Rep. 2019 Aug 7;9(1):11433. doi: 10.1038/s41598-019-47389-w.

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Laboratory of Genomic Instability in Development and Disease

Group Leader: Floris Foijer

1. Bolhaqueiro ACF, Ponsioen B, Bakker B, Klaasen SJ, Kucukkose E, van Jaarsveld RH, Vivié J, Verlaan-Klink I, Hami N, Spierings DCJ, Sasaki N, Dutta D, Boj SF, Vries RGJ, Lansdorp PM, van de Wetering M, van Oudenaarden A, Clevers H, Kranenburg O, Foijer F, Snippert HJG, Kops GJPL (2019) Ongoing chromosomal instability and karyotype evolution in human colorectal cancer organoids. Nat Genet. 2019 May;51(5):824-834. doi: 10.1038/s41588-019-0399-6. Epub 2019 Apr 29.

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9. Preprint: Single cell DNA sequencing reveals distinct molecular types of basal cell carcinoma with unique transcriptome features Bjorn Bakker, Jorrit Terra, Lin Zhou, Emoke Racz, Sonja Paljic, Jorge Garcia-Martinez, Vera Oliveira, Petra L Bakker, Diana C.J. Spierings, Marcel F. Jonkman, Floris Foijer bioRxiv 492199; doi: https://doi.org/10.1101/492199

10. Preprint: Altering microtubule dynamics is synergistically toxic with inhibition of the spindle checkpoint Klaske M. Schukken, Yi-Chih Lin, Michael Schubert, Stephanie F. Preuss, Judith E. Simon, Hilda van den Bos, Zuzana Storchova, Maria Colome Tatche, Holger Bastians, Diana C.J. Spierings, Floris Foijer bioRxiv 706077; doi: https://doi.org/10.1101/706077

Laboratory of Ageing Biology and Stem Cells

Group Leader: Gerald de Haan

1. Buisman SC, de Haan G.(2019) Epigenetic Changes as a Target in Aging Haematopoietic Stem Cells and Age-Related Malignancies. Cells. 2019 Aug 10;8(8). pii: E868. doi: 10.3390/cells8080868.

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Laboratory of Macromolecules and Interactomes

Group Leader: John LaCava

1. Ardeljan D, Wang X, Oghbaie, Taylor MS, Husband D , Deshpande V, Steranka JP, Gorbounov M, Yang WR, Sie B, Larman HB, Jiang H, Molloy KR, Altukhov I, Li Z, McKerrow W, Fenyö D, Burns KH, LaCava J. (2019)LINE-1 ORF2p expression is nearly imperceptible in human cancers. doi: https://doi.org/10.1101/744425

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4. Preprint: Oghbaie M, Šulc P, Fenyö D, Pennock M, LaCava J (2019) Complex+: Aided Decision-Making for the Study of Protein Complexes. doi: https://doi.org/10.1101/744656

Laboratory of Cellular Biochemistry

Group Leader: Liesbeth Veenhoff

1. Mishra A, Sipma W, Veenhoff LM, Van der Giessen E, Onck PR. (2019) The Effect of FG-Nup Phosphorylation on NPC Selectivity: A One-Bead-Per-Amino-Acid Molecular Dynamics Study.Int J Mol Sci. 2019 Jan 30;20(3). pii: E596. doi: 10.3390/ijms20030596.

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Laboratory of Cellular Senescence and Age-related Pathologies

Group Leader: Marco Demaria

1. Soto-Gamez A, Quax WJ, Demaria M (2019) Regulation of Survival Networks in Senescent Cells: From Mechanisms to Interventions. J Mol Biol. 2019 Jul 12;431(15):2629-2643.doi: 10.1016/j.jmb.2019.05.036. Epub 2019 May 31.

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Laboratory of Telomeres and Genome Integrity

Group Leader: Michael Chang

1. Novarina D, Janssens GE, Bokern K, Schut T, van Oerle NC, Kazemier HG, Veenhoff LM,Chang M (2019) A genome-wide screen identifies genes that suppress the accumulation of spontaneous mutations in young and aged yeast cells. Ageing cell* 19(2), [e13084]. https://doi.org/10.1101/492587

Laboratory of Genetic Instability and Ageing

Group Leader: Peter Lansdorp

1. Bolhaqueiro ACF, Ponsioen B, Bakker B, Klaasen SJ, Kucukkose E, van Jaarsveld RH, Vivié J, Verlaan-Klink I, Hami N, Spierings DCJ, Sasaki N, Dutta D, Boj SF, Vries RGJ, Lansdorp PM, van de Wetering M, van Oudenaarden A, Clevers H, Kranenburg O, Foijer F, Snippert HJG, Kops GJPL (2019) Ongoing chromosomal instability and karyotype evolution in human colorectal cancer organoids. Nat Genet. 2019 May;51(5):824-834. doi: 10.1038/s41588-019-0399-6. Epub 2019 Apr 29.

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Laboratory of Genome Structure Ageing

Group Leader: Victor Guryev

1. Mahmud H, Ter Elst A, Scherpen FJG, Boer TM, Kampen KR, de Haas V, Guryev V, Peppelenbosch MM, Kornblau SM, de Bont ESJM. (2019) Peptide microarray of pediatric acute myeloid leukemia is related to relapse and reveals involvement of DNA damage response and repair. Oncotarget. 2019 Jul 23;10(45):4679-4690. doi: 10.18632/oncotarget.27086. eCollection 2019 Jul 23.

2. Boudewijn IM, Lan A, Faiz A, Cox CA, Brouwer S, Schokker S, Vroegop SJ, Nawijn MC, Woodruff PG, Christenson SA, Hagedoorn P, Frijlink HW, Choy DF, Brouwer U, Wisman M, Postma DS, Fingleton J, Beasley R, van den Berge M, Guryev V. (2019) Nasal gene expression changes with inhaled corticosteroid treatment in asthma. Allergy. 2019 Jun 22. doi: 10.1111/all.13952. [Epub ahead of print]

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5. Faiz A, van den Berge M, Vermeulen CJ, Ten Hacken NHT, Guryev V, Pouwels SD (2019) AGER expression and alternative splicing in bronchial biopsies of smokers and never smokers. Respir Res. 2019 Apr 10;20(1):70. doi: 10.1186/s12931-019-1038-6.

6. Ng-Blichfeldt JP, de Jong T, Kortekaas RK, Wu X, Lindner M, Guryev V, Hiemstra PS, Stolk J, Königshoff M, Gosens R (2019) TGF-β activation impairs fibroblast ability to support adult lung epithelial progenitor cell organoid formation. Am J Physiol Lung Cell Mol Physiol. 2019 Jul 1;317(1):L14-L28. doi: 10.1152/ajplung.00400.2018. Epub 2019 Apr 10.

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8. Ong J, Woldhuis RR, Boudewijn IM, van den Berg A, Kluiver J, Kok K, Terpstra MM, Guryev V, de Vries M Vermeulen CJ , Timens W, van den Berge M, Brandsma CA. (2019) Age-related gene and miRNA expression changes in airways of healthy individuals. Sci Rep. 2019 Mar 6;9(1):3765. doi: 10.1038/s41598-019-39873-0.

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10. van den Bos H, Bakker B, Taudt A, Guryev V, Colomé-Tatché M, Lansdorp PM, Foijer F, Spierings DCJ.(2019) Quantification of Aneuploidy in Mammalian Systems. Methods Mol Biol. 2019;1896:159-190. doi: 10.1007/978-1-4939-8931-7_15.

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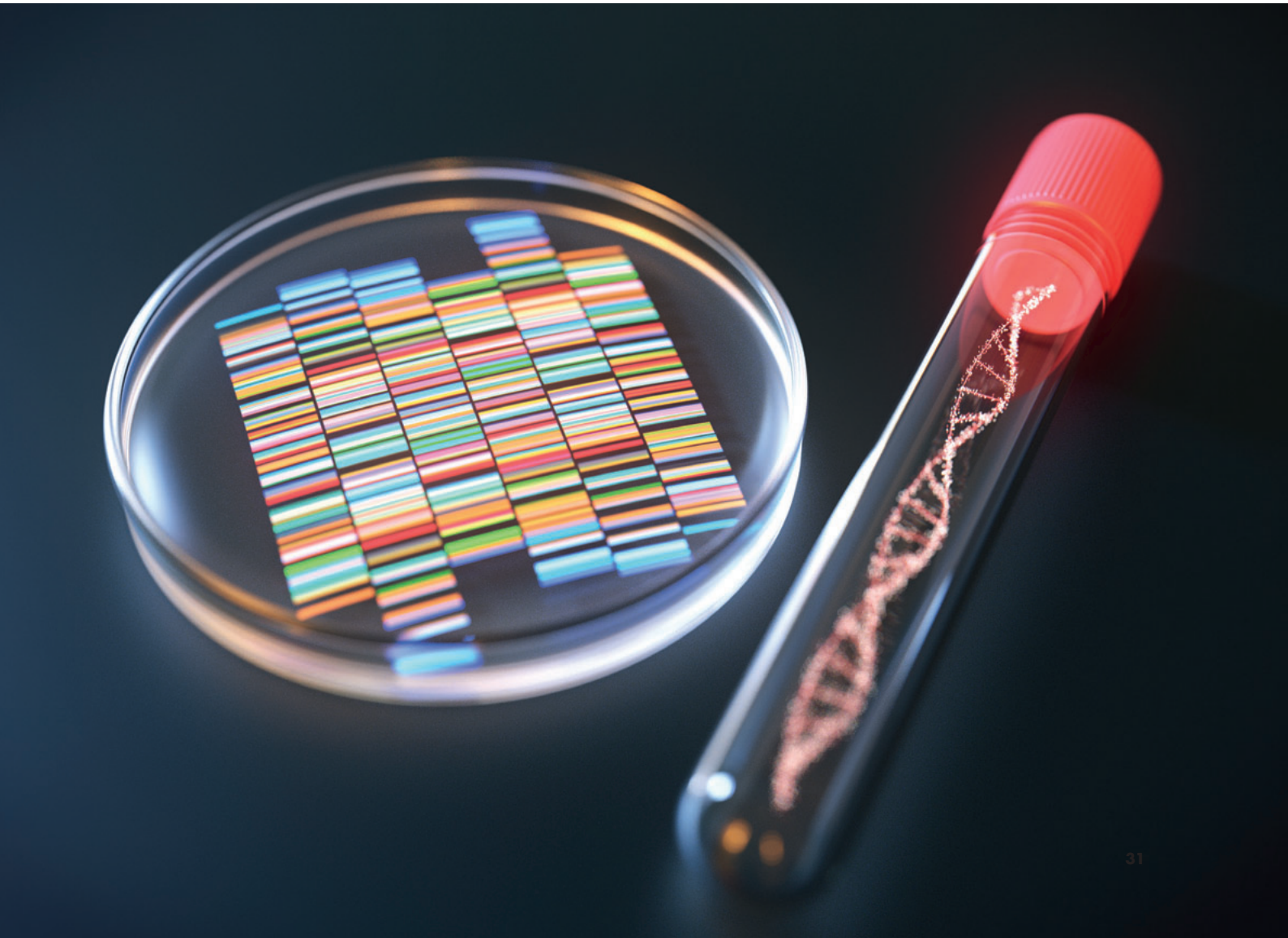
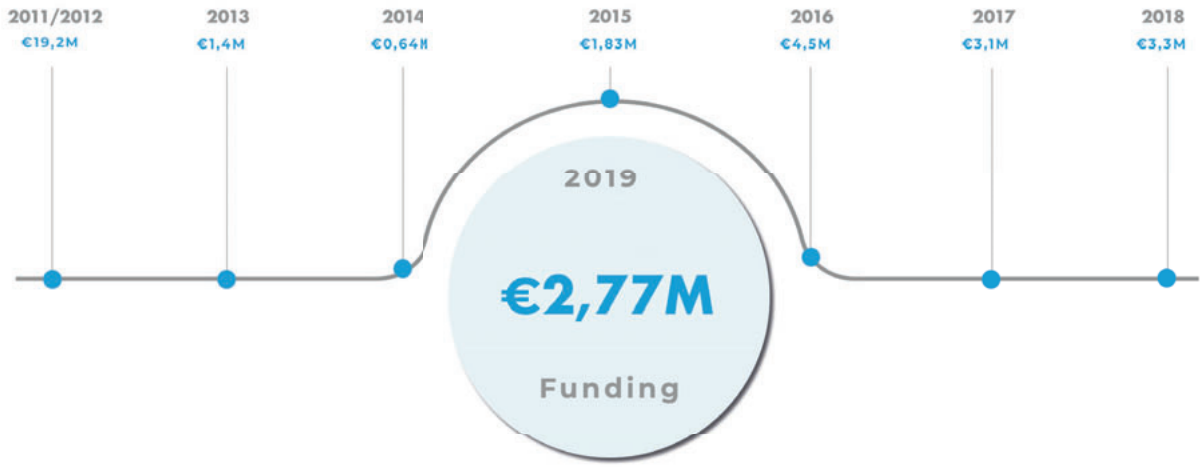
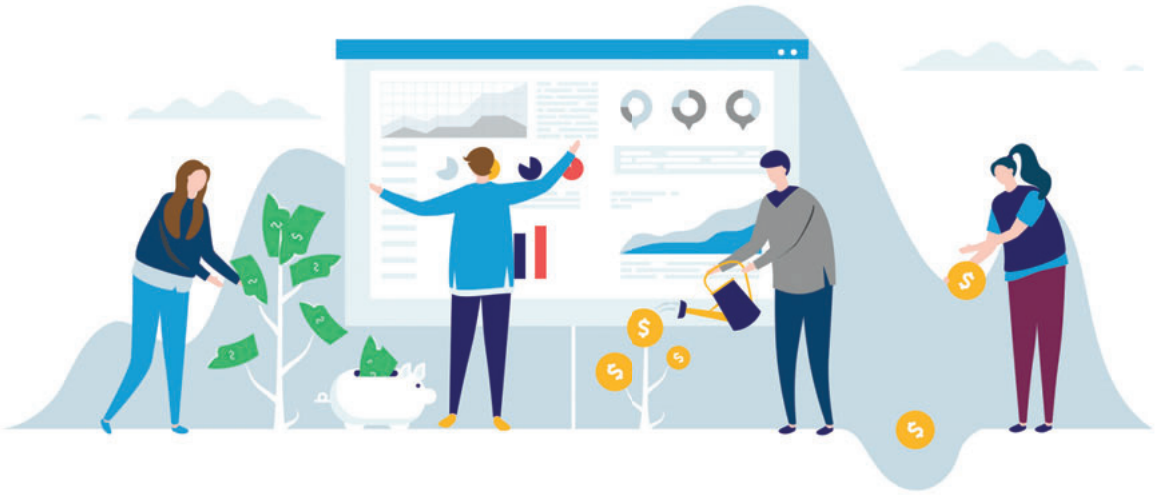
*Preprints included in 2018 annual report are now published.
Out of 61 publications, five are preprints.



Funding/Grants





Research proposals awarded in 2019

Principal Investigator/ Researcher	Role	Grant	Title	Budget
Amanda Assoni	Applicant	De Cock	Restoring VAPB levels in iPS –derived motor neurons from ALS patients	€ 3.500
Christy Hong	Applicant	De Cock	Investigation of the underlying biology behind nuclear localization of cGAS in breast cancer cells	€ 3.500
ThijmenVan Vliet	Appilcant	De Cock	caloric restriction to reduce toxicity of chemotherapy-induced senescence	€ 3.500
Britt Sterken	Applicant	De Cock	The role of the C/EBPβ isoforms in breast cancer	€ 3.500
Inna Armandari	Applicant	De Cock	Understanding the Role of KMT2D in Sonic Hedgehog Medulloblastoma	€ 3.500
Marco Demaria	Co-applicant	ZonMw publiek-private partnerships: Parkinson en Vitaliteit & Levensloop	SMARTage; part of Vitality Oriented Innovation for the Lifecourse of the Ageing Society (VOILA)	€ 758.850
Eugene Berezikov	Applicant	ENW-KLEIN-set 02	Stem cell differentiation programs in the regenerative flatworm Macrostomum Lignano	€ 359.373
Gerald de Haan	Applicant	KWF	Characterizing and targeting CBX7 regulated selfrenewal pathways in leukemia	€ 615.000
Floris Foijer	Applicant	KWF	ScreeninC: a national infrastructure for functional genome editing and large scale funtional screening	€ 600.000

Principal Investigator/ Researcher	Role	Grant	Title	Budget
John LaCava	Applicant	Public-Private Partnership, Health Holland	Affinity capture / mass spectrometry screening combined with mass photometry to assess sample heterogeneity and predict macromolecular topologies	€ 76.800
John LaCava	Applicant	Kanker Research Fonds	Targeted mass spectrometry detection of a parasitic gene product in human cancers	€ 3.000
Ellen Nollen	Applicant	ALS Foundation	Discovering therapeutic targets to rescue motor impairment using small animal model for ALS (SMALLS)	€ 208.000
Sahil Gupta	Applicant	DFG	Mapping the initiating steps of aneuploidy and aneuploidy tolerization in tumorigenesis	€ 67.008
Lin Zhou	Applicant	KRF	Finding the drivers of aneuploidy-induced senescence	€ 3.000
Siqi Zeng	Applicant	CSC	The consequences of chromosomal instability during development and in tumorigenesis in zebrafish	€ 64.800

KWF: Dutch Cancer Society
NWO: Netherlands Organisation for Scientific Research
De Cock: Jan Kornelis de Cock Foundation
UMCG: University Medical Center Groningen/Cancer Research Funds
ALS Foundation: Amyotrophic lateral sclerosis Foundation
CSC: Chinese Scholarship Council

Invited Speakers

In 2019, many eminent scientists have been invited to give talks and lectures in ERIBA and University Medical Center Groningen.

Speaker	Host	Title of talk/lecture	University / Institute	Event
Iris Jonkers	Gerald de Haan	Beyond GWAS - understanding how genetically associated regions contribute to celiac disease "	Department of Genetics, UMCG	Friday afternoon meeting
Hans Jonker	Gerald de Haan	Fibroblast Growth Factors in the regulation of metabolic healthspan and lifespan"	Department of Pediatrics, UMCG	Friday afternoon meeting
George Janssen	Michael Chang	Going from 'omics' data to therapeutics: a focus on aging"	AMC in Amsterdam	Friday afternoon meeting
Peter van der Meer	Gerald de Haan	" Identification of novel targets in heart failure"	Department of Cardiology and Thorax Surgery, UMCG	Friday afternoon meeting
Peter Adams	Marco Demaria	The dynamic epigenome - a challenge for healthy aging	Sanford Burnham Prebys Medical Discovery Institute, La Jolla CA, USA	Molecular Medicine Series
Burkhard Becher	Marco Demaria and Jon Laman	The T cell/phagocyte interface during chronic inflammation	ETH, Zürich, Switzerland	Molecular Medicine Series
Shelley Buffenstein	Gerald de Haan	Bare essentials of aging; a naked mole rat perspective	Calico, San Francisco, USA	Molecular Medicine Series

Speaker	Host	Title of talk/lecture	University / Institute	Event
Adnan Halim	John LaCava	Protein O-glycosylation in human health and disease	Center for Glycomics (CCG), University of Copenhagen, Denmark	Molecular Medicine Series
Bernhard Schmierer	Floris Foijer and Jonas Seiler	Pooled CRISPR/Cas9 genetic screening: methods, applications and an unexpected finding	High Throughput Genome Engineering, National Facility | Science for Life Lab, Stockholm, Sweden	CRISPR/Cas9 Technology Symposium
Michael Ristow	Cor Calkhoven	Metabolic Control of Healthy Aging	ETH Zürich, Switzerland	Molecular Medicine Series
Nanette Jellema	Floris Foijer	The impact of distinct levels of chromosomal instability on cancer"	Hubrecht institute	Friday afternoon meeting
Jeroen Bakkers	Eugene Berezikov and Judith Paridaen	Heart regeneration: lessons from zebrafish	Hubrecht Instituut, Utrecht	Molecular Medicine Series
Eline Slagboom		Metabolic profiling of human health, ageing and mortality	Leiden University, The netherlands	3rd Biology of Ageing meeting 2019
Stephen Simpson		The Nutritional Geometry of Aging and Metabolic Health	The University of Sydney, Australia	3rd Biology of Ageing meeting 2019
Maria Teresa Teixeira		Telomeres and the route to senescence	CNRS, France	3rd Biology of Ageing meeting 2019
Jan Vijg		Single-cell analysis of genome instability in ageing	Albert Einstein College of medicine, United States of America	3rd Biology of Ageing meeting 2019
Francis Rodier		Irreversible genome damage from teomeric fusions estblish replicative senescence in normal human cells	CRCHUM, Canada	3rd Biology of Ageing meeting 2019

Speaker	Host	Title of talk/lecture	University / Institute	Event
Marie Noelle Simon		The nuclear pore complex prevents sister chromtid recombination at telomeres during replicative senescence	CNRS, France	3rd Biology of Ageing meeting 2019
Titia de Lange		Telomeres and cancer:tumor suppression and genome instability	The Rockefeller University, united States of America	3rd Biology of Ageing meeting 2019
Toren Finkel		Mitochondria, metabolism and ageing.	University of Pittsburgh, United States of America	3rd Biology of Ageing meeting 2019
Patricia Boya		Autophagy in neurons:from development to aging	CSIC, Madrid, Spain	3rd Biology of Ageing meeting 2019
Riekelt Houtkooper		Cross-compartmental proteostasis in longevity	University Medical Center Amsterdam, The Netherlands	3rd Biology of Ageing meeting 2019
Natascia Ventura		Mitochondrial bionergetic changes during development as an indicator of C. elegans health-span	Heinrich Heine University, Germany	3rd Biology of Ageing meeting 2019
Peter Adams		Mitochondrial-nuclear retrograde signaling drives senescence-associated infmamation and is a target for healthy aging	Sanford Burnham Prebys Medical Discovery Institute, United States of America	3rd Biology of Ageing meeting 2019
Christof Niehrs		DNA demethylation and aging	Institute of Molecular Biology, Germany	3rd Biology of Ageing meeting 2019
Tamir Chandra		Global changes accompany and distinguish primary and secondary senescence induction	The University of Edinburgh, United Kingdom	3rd Biology of Ageing meeting 2019
Jan van Deursen		Understanding in vivio senescence to improve healthy aging	Mayo Clinic, United States Of Americ	3rd Biology of Ageing meeting 2019

Speaker	Host	Title of talk/lecture	University / Institute	Event
Manuel Collado		Identifying novel senelotic compounds by high throughput screening	Health Research Institue of Santiago de Compostela (IDIS) Spain	3rd Biology of Ageing meeting 2019
Ines Sturmlechner		Senescent cells uncouple p21 from p53 to sustain cell viability, cell cycle arrest and immunosurveillance.	Mayo Clinic, united States of America	3rd Biology of Ageing meeting 2019
Christiaan Leeuwen burgh		Clinical Trials Originated from Findings from Biolgy of Aging Research	University of Florida	3rd Biology of Ageing meeting 2019
Richard Cawton		Lower germline mutation rates in young adults predict longer lives and longer reproductive lifespans	University of Utah, United States of America	3rd Biology of Ageing meeting 2019
Yves Barral		Ageing: some insights from a good old fungus	Institute of Biochemistry/ ETH Zurich, Switzerland	3rd Biology of Ageing meeting 2019
Simon Alberti		Phase seperation as astress survival strategy	Max Planck Institute of Molecular Cell Biology and Genetics, Germany	3rd Biology of Ageing meeting 2019
Sebastian Iben		A novel pathomechanism:are Cockayen syndrome and trichothiodystrophy ribosomopathies?	University of Ulm, Germany	3rd Biology of Ageing meeting 2019
Martin Denzel		Activation of eID=F2B? Extends lifespan in C.elegans by promoting selective mRNA translation	Max Planck Institute for Biology of Ageing, Germany	3rd Biology of Ageing meeting 2019
Patrick van der Wel		Molecular structure and biological activity of protein aggregates assocated with huntington disease	Zernike Institute for Advanced Materialse, The Netherlands	3rd Biology of Ageing meeting 2019
Hiromitsu Nakauchi		Growing organs in vivo:iPS cell-derived, xeno-created organs for transplantation	Stanford University, United states of America	3rd Biology of Ageing meeting 2019

Speaker	Host	Title of talk/lecture	University / Institute	Event
Claudia Waskow		Prospective isolation of the non-hematopoietic stem cell niche and its molecular cross-talk to hemaopoietic stem cells	Leibniz-Institute on Aging, D=Fritz-Lipmann-Institute (FLI), Germany	3rd Biology of Ageing meeting 2019
Ruzhica Bogeska		Repetitive Exposure to inflammatory Stress Leads to Hematopoietic Stem Cell Atriition and Hematopoietic Tissue Failure during Ageing	German Cancer Research Center (DKFZ), Germany	3rd Biology of Ageing meeting 2019
Kristina Kirschner		Age-related clonal haemopoiesis and myeloproliferative disease are associated with increased epigenetic age	University of Glasgow, United Kingdom	3rd Biology of Ageing meeting 2019
Lenhard Rudolph		Mitochondrial dysfunction limits metabolic plasticity of aging stem cells to adapt to changes in nutrient availibility	Leibniz Institute on Aging-FLI, Germany	3rd Biology of Ageing meeting 2019
Matt Kaeberlein		Targeting aging through mTOR inhibition	University of Washington, United States of America	3rd Biology of Ageing meeting 2019
Prof. Robert W Williams	Victor Guryev	Workshop on GeneNetwork - online platform for multiomics data integration"	University of Tennessee	extra seminar/ defense Tristan de Jong
Ben Giepmans		Optogenetic modulation of exocrine cells leading to beta cell stress in zebrafish	Biomedecial Sciences and Cell Systems, UMCG	Fish Technologie symposium
Luiza Reali Nazario		PET imaging in zebrafish	Nuclear Medicine, UMCG	Fish Technologie symposium

Speaker	Host	Title of talk/lecture	University / Institute	Event
Jeroen Bakkers		Haert regeneration:lessons from zebrafish	Hubrecht Institute for Development Biology and Stem Cell Research, Utrecht	Fish Technologie symposium
Catriene Thuring		Introduction CDP Fish Facilities	CDP, UMCG	Fish Technologie symposium
Fabrizio d'Adda di Fagagna		DNA damage response in aging and its control by non coding RNA	IFOM, Milan, Italy	Marco Demaria
Lluis Morey	John LaCava	Role of polycomb complexes in stem cells and cancer	Sylvester Comprehensive Cancer Center, Cancer Epigenetics Program, Dept. Of Human Genetics, University of Miami, Miller School of Medicine, Miami, USA	Molecular Medicine Series

People

EMPLOYEES

2019

99

2013 - 81
2014 - 89
2015 - 89
2016 - 92
2017 - 107
2018 - 100

STAFF MEMBERS UNDER 40

2019

73%

2013 - 69%
2014 - 63%
2015 - 63%
2016 - 61%
2017 - 76%
2018 - 72%

FEMALE EMPLOYEES

2019

62%

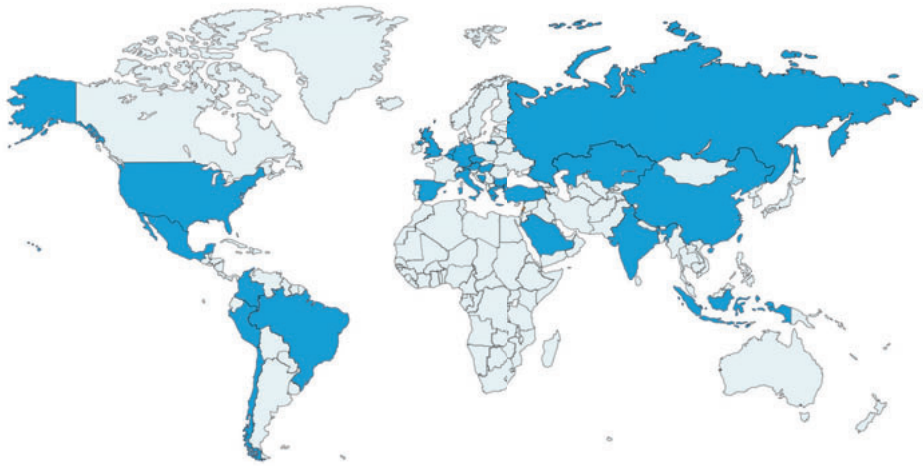
2013 - 60%
2014 - 56%
2015 - 56%
2016 - 55%
2017 - 54%
2018 - 60%

INTERNS

2019

48

2013 - 17
2014 - 41
2015 - 41
2016 - 26
2017 - 49
2018 - 45



NUMBER OF NATIONALITIES

27

BOSNIA AND HERZEGOVINA
UNITED KINGDOM
HONGKONG
RUSSIA
PERU
BELGIUM
TURKEY
USA
CHINA
CZECH REPUBLIC
THE NETHERLANDS
GERMANY
SAUDI-ARABIA
KAZAKHSTAN
INDIA
CHILE
GREECE
MEXICO
SPAIN
BRAZIL
ITALY
LEBANON
BULGARIA
INDONESIA
HUNGARY
AUSTRIA
COLOMBIA

INTERNATIONALS

2019

49%

2013 - 47%
2014 - 48%
2015 - 47%
2016 - 45%
2017 - 49%
2018 - 46%

DOCTORAL STUDENTS HOSTED BY ERIBA

2019

26

2013 - 22
2014 - 22
2015 - 26
2016 - 27
2017 - 44
2018 - 39

(10 of these students hosted by ERIBA under the GSMS Bursary Scheme)

MANAGEMENT TEAM ERIBA

Henk Heidekamp, Managing Director
Arnoud Rozema, Staff Advisor
Kevin Huizinga, Financial Controller
Megha Upadhyay-Pandey, Research Coordinator
Nina Kool, Research Development Office Assistant
Annet Vos-Hassing, Secretary
Sylvia Hoks, Secretary
Alida de Haan, Secretary
Yin Fai Chan, Technician (general support)

Facilities

Education

Outreach & Dissemination

Scientific Advisory Board

Sponsors

Facilities

iPSC/CRISPR

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 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. We expect to accommodate several new large-scale projects, as we appointed more postdocs, 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 - Posdoctoral Fellow

Sahil Gupta - Postdoctoral Fellow

Jonathan Seiler - Postdocoral Fellow

Mathilde Broekhuis - Technician

Eslie Huizinga - Technician

Contact

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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 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

Central Animal Facility (CDP) UMCG
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The Netherlands

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Sequencing Facility

Next generation sequencing (NGS) technology is revolutionizing medicine and life sciences and has become a routine tool to assess the genomes, epigenomes and transcriptomes of cultured cells, (liquid) biopsies, and primary tissue/disease samples. In May 2019, the Research Sequencing Facility was officially established within the ERIBA Technology Center, as a dedicated research infrastructure to provide support for NGS-based projects for UMCG and RUG research groups. For this, we will not only facilitate the expeditious sequencing of NGS libraries either prepared by research groups themselves or by the facility on behalf of the researcher, but also implement the latest NGS techniques used in medicine and life sciences research, and (co)develop and implement new state-of-the-art NGS techniques to keep NGS-dependent research in the UMCG at the forefront. Furthermore, we advise the researchers on the set-up of their NGS experiments and train researchers in the production of NGS libraries if they would prefer to do this themselves. As a spin-off from the Peter Lansdorp research group, we are experts in single-cell DNA sequencing and the only sequencing facility offering the Strand-seq technology as a service. Strand-seq is a powerful tool to identify besides copy number alterations also copy-number neutral structural genomic aberrations such at inversions and translocations, all at the single cell level thereby preserving tissue heterogeneity. In 2019, we have generated over 14,000 single-cell DNA-seq libraries derived from approximately 340 different samples. Moreover, we facilitated ~100 sequencing runs in total. Although we could only facilitate small NGS projects (RNA-seq, ATAC-seq, DNA-seq) in 2019, we expect to accommodate many new large-scale projects as we have invested in infrastructure to automate library preparation thereby drastically increasing our capacity for many NGS applications.

Who

Diana Spierings – Coordinator Research Sequencing Facility

Nancy Halsema – Technician

Karina Wakker-Hoekstra – Technician

Jennefer Beenen – Technician

Contact

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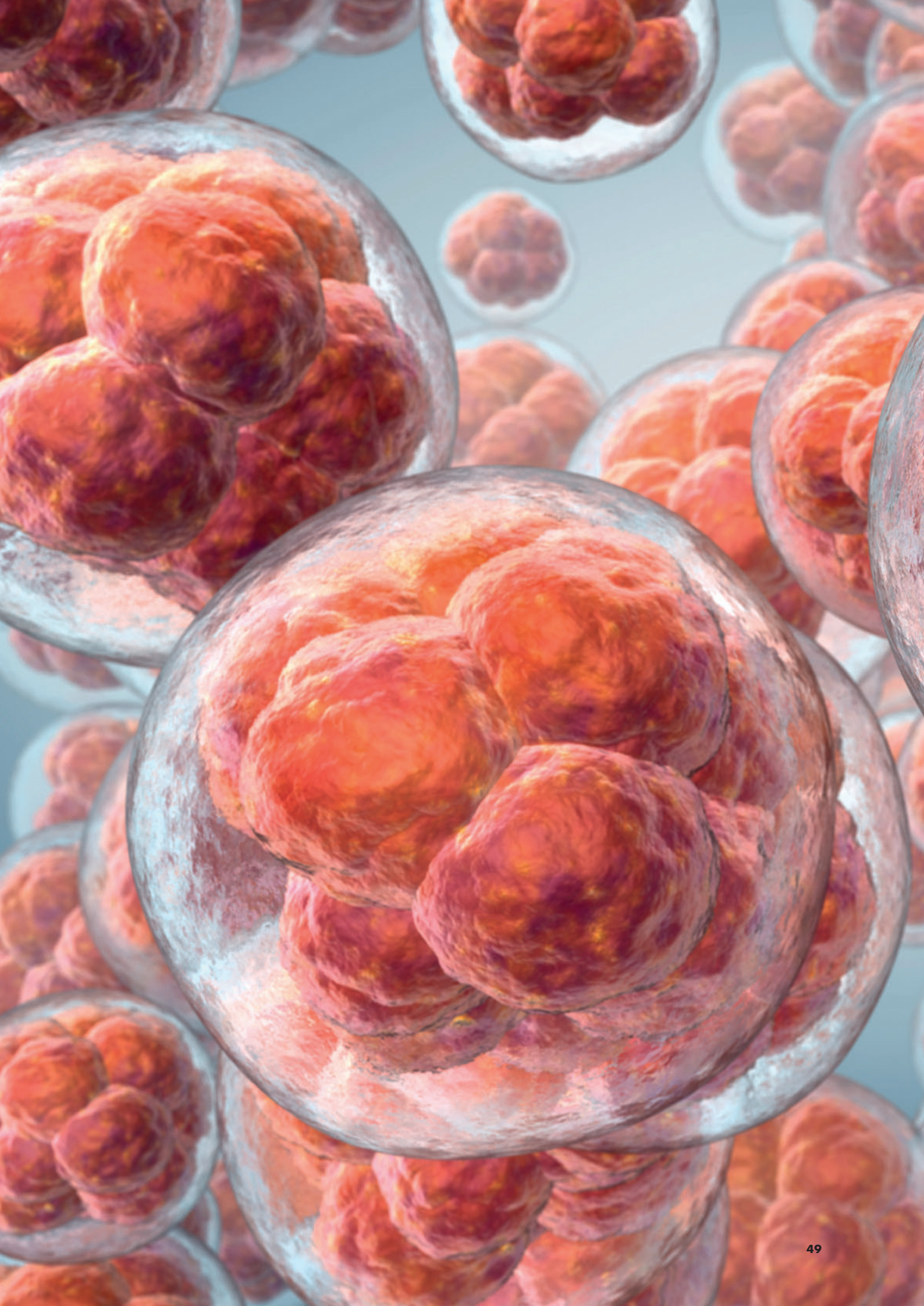


Education

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 ERIBA

10 ECTS, 20 BSc. Biology, and Life Science and Technology students

Coordinator: Cor Calkhoven

Objectives: A laboratory research course with research topics covering 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, and bioinformatics.

CRISPR genome engineering

5 ECTS; 30 students

Coordinator: Floris Foijer

Objectives: In this course, MSc learn the basics of CRISPR engineering. Students learn about the history and various applications of CRISPR including knockouts, knockins, CRISPR I, CRISPRa, mutations and genome-wide screens. Furthermore, they get hands-on experience in the design of guide RNAs and genome editing tools and apply them in the lab. Finally, they combine their newly acquired expertise in an assignment in which they design a complete CRISPR strategy for a fictive project.

Models systems in Ageing research

3 ECTS; 4 students (2019), 8 students (2020)

Coordinator: Floris Foijer

Objectives: In this JSM course, third year medical students explore fundamental biology and are exposed to several of the model organisms we use at ERIBA for ageing-related research. Students discuss advantages and disadvantages of the model organisms with researchers on the lab. and study relevant papers that make use of the model organisms. In small groups, they compare the feasibility of 2-3 models Ito study (aspects of) a particular disease and discuss the advantages and disadvantages of these models in this setting.

Specialization Track on the Biology of Ageing

Master students in Biomedical Sciences (FWN), 21 students

Coordinator: Ellen Nollen/Floris Foijer

Objectives: Coordination and mentoring of student that want to specialize in ageing research. The research track includes courses have been developed and are coordinated by ERIBA PIs, which are i) Molecular Biology of Ageing course, ii) Current themes in Healthy Ageing, and iii) CRISPR genome engineering.

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.

Exam committee Behavioural and Cognitive Neuroscience Research Master (BCN-ReMa)

Member, Secretary; Liesbeth Veenhoff

The board of examiners assesses the results of teaching for individual BCN-ReMa students, and guarantees the quality of examinations and final assessments.

Opleidingscommissie Molecular Medicine and Innovative Treatment (MMIT)

Member: Liesbeth Veenhoff

The program committee gives advice to ensure the quality of the educational program.

Current Themes in Healthy Ageing

5 ECTS, 10 MSc Biomedical Sciences students

Coordinators: Marco Demaria and Judith Paridaen

Objectives: Learn leading edge ageing research and interact with prominent ageing scientists by following scientific seminars. Biomedical Science students attend 7- scientific seminars and report on content, scientific excellence and track records of the presenters. This course has 10-30 students/year.

Python in biology for beginners

EC 1, 20 PhD students in biology, medical biology, medicine or farmacy- those who professionally connected to biology.

Course coordinator: Leonid Bystrykh

Introductionary course on python for biologists, include basic grammar, operations with files, use of statistical functions, making scientific illustrations, analysing images.

Objectives: Biologists are traditionally educated in programming-free environment. This causes serious limitations in the ability to collect, process and understand the data they create or use from others. Python is universal and relatively simple programming language, one of the most popular in science at this time. Among others, it contains biological packages. Regretfully, many biologists are not aware of this fact. Many python tutorials are based on examples, which do not appeal to biology or medical students. In this course I make an adaptation of selected python packages for biological applications.

Knowing this language will improve the ability of students to process, analyze and understand their and other's data. This is essential for proper development of the young scientists.

Genome data for beginners and advanced

EC 1, 20 GSMS PhD students (including BCN PhD students)

Course coordinator: Leonid Bystrykh

Objectives: Data retrieval from public databases, use of R and python scripts for the analysis of data. Gene expression data processing for microarrays, bulk RNAseq data and single-cell RNA-seq

To increase the understanding of the basic principles of bioinformatics and to gain practical skills in bioinformatics analysis of sequence data.

Python for biologists

May 2019, organized at Karolinska Institute in Stockholm, Sweden

20 participants

Coordinators: Dr. Leonid Bystrykh and Dr. Victor Guryev

Introductionary course on python for biologists, include basic grammar, operations with files, use of statistical functions, making scientific illustrations, analysing images.

Genome biology

September 2019, organized at Karolinska Institute in Stockholm, Sweden

19 doctoral students

Coordinators: Dr. Leonid Bystrykh and Dr. Victor Guryev

Data retrieval from public databases, use of R and python scripts for the analysis of data. Gene expression data processing for microarrays, bulk RNAseq data and single-cell RNAseq

To increase the understanding of the basic principles of bioinformatics and to gain practical skills in bioinformatics analysis of sequence data.

Outreach and Dissemination

ERIBA is committed to outreach and dissemination activities. To this cause, ERIBA personnel consistently take part in various communication and outreach activities. This is to ensure that general public is well aware of the research activities in ERIBA. Such activities also bring general public closer to research and generates a lot of enthusiasm in kids to become the scientists of tomorrow. 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. Public events, activities for schools, tours and many more initiatives are taken to achieve the goals.

Some of our most notable activities are listed below

Media

- Victor Guryev's article was published in the Kijk (magazine) in the March 2019 edition. The title was "In de donkere krochten van DNA" where he described his research which uses state-of-art bioinformatics tools to figure "hard to find genes" (dark DNA).

- Research from an international team, including Peter Lansdorp and Victor Guryev from ERIBA in Groningen, published in Nature communications made headlines in ukrant (www.ukrant.nl). The team discovered structural differences in the DNA of individuals. "Lansdorp's technique single-cell strand seq technology) can view the entire chromosome," says Guryev. "In addition, you can distinguish between the chromosomes inherited from the father and from the mother, which is impossible with other techniques."

- Gerald de Haan's Interview was published in Volkskrant (https://www.volkskrant.nl/wetenschap/vreemd-medicijncocktail-maakt-ouderen-biologisch-jonger~bc55a067/) about rejuvenation of blood. Here, he discussed the importance and a surprise finding by researchers of boosting the immune system of individuals. This boost resulted in older becoming younger by two years.

  Interview RTL Editie NL
  Interview Radio1: Verjonging van bloed

- On June 13, at the occasion of the 405th anniversary of the University of Groningen, an honorary doctorate was awarded to professor Titia de Lange (Rockefeller University). Titia de Lange has made seminal contributions in the field of cancer and ageing biology. She was interviewed by Janine Abbring (VPRO tv programme Zomergasten) where she talked about life, work, and science. Gerald de Haan acted as the honorary promotor.

- Judith Paridaen was elected as one of the members of Young Academy Groningen. It is a club for the University of Groningen's most talented, enthusiastic and ambitious young researchers. A video with Judith describing
  her stem cell research was posted on youtube (https://www.youtube.com/watch?v=xHVe3MTg6ZM) by the University of Groningen

Events /Activities

Career Day

Members Involved:
Judith Paridaen, Katya Dvorianinova, Anita Pras, Megha Upadhyay, Sylvia Hoks

Career Day was organised on the April 24th 2019. Approx 70 people attended the event. The event featured presentations from people from various disciplines. The speakers shared their experience and provided advice to students on careers outside academia. Mate Palfy Community Manager Prelights, inititative of The company of Biologists, Cambridge, UK, Seong-Joo Koo Discovery Scientist Janssen pharmaceutical company, Belgium, Maxime Willems Founder of Foodlab 'Proef!' and Business Developer for InvertTox, Ghent, Paula van Tijn Institute Manager AMOLF, Amsterdam, Marnix Wieffer Senior Marketing Manager Drug Safety at Elsevier, The Netherlands, Annemieke van der Goot Consultant at Vindsubsidies (Idox Grants BV), The Netherlands, Eva Teuling Education Coordinator at the University of Groningen, Groningen. The event was a huge success and will again be held in 2021.

Zpannend Zernike

Staff members involved:
Organiser: Anton Steen
Volunteers: Judith Paridaen, Katya Dvorianinova, Liesbeth Veenhoff, Marije Semmelink, Sylvia Hoks, Alida de Haan, Leen Janssen, Sabrina Jacobs, Danielle Luinenburg, Megha Upadhyay, Jacob Wudarski, Gloria Casas Gimeno.

ERIBA is committed to public outreach activities and wants to create public awareness on scientific research, inspire scientists of tomorrow. The "Weekend van de Wetenschap" locally known as Zpannend Zernike is an event in which research institutes, the University of Groningen, the UMCG, and the Hanze Hogeschool team up in Groningen as a single organization organizing scientific activities for primary school children and their families. ERIBA also participated in this event and opened its doors to the public. On Saturday, the 5th of October, 2019 more than 680 people visited the ERIBA premises and took part in various scientific activities. The activities included isolation of DNA, exploring model organisms used for scientific research, Healthy ageing quiz, a scientific escape room, and diving in dates session. These activities generated a lot of enthusiasm and enlightened the public on the importance of science and scientific research,

3rd Molecular Biology of Ageing Meeting

Members involved:
Gerald de Haan, Cor Calkhoven, Liesbeth Veenhoff, Megha Upadhyay, Nina Kool, Sylvia Hoks, Annet Vos-Hassing, Alida de Haan, Kevin Huizinga, Eleni Fitsiou, Gertrud Kortman, Gloria Casas Gimeno, Eniko Fekete- Szucs, Danielle Luinenburg,

ERIBA successfully organized for the third time the Molecular Biology of Ageing (www.bioageing.nl) Meeting, focusing on ageing research. The meeting was held from October 10-12, 2019, at the University Medical Center Groningen. The organizing committee brought together world-leading scientists to discuss the diverse research areas that are relevant for understanding the biology of ageing. To 'build the scientists of tomorrow' the 'meet the expert' session was also organized where PhD students and young scientists interacted with the experts to gain knowledge from their experiences.

Science activities and visits

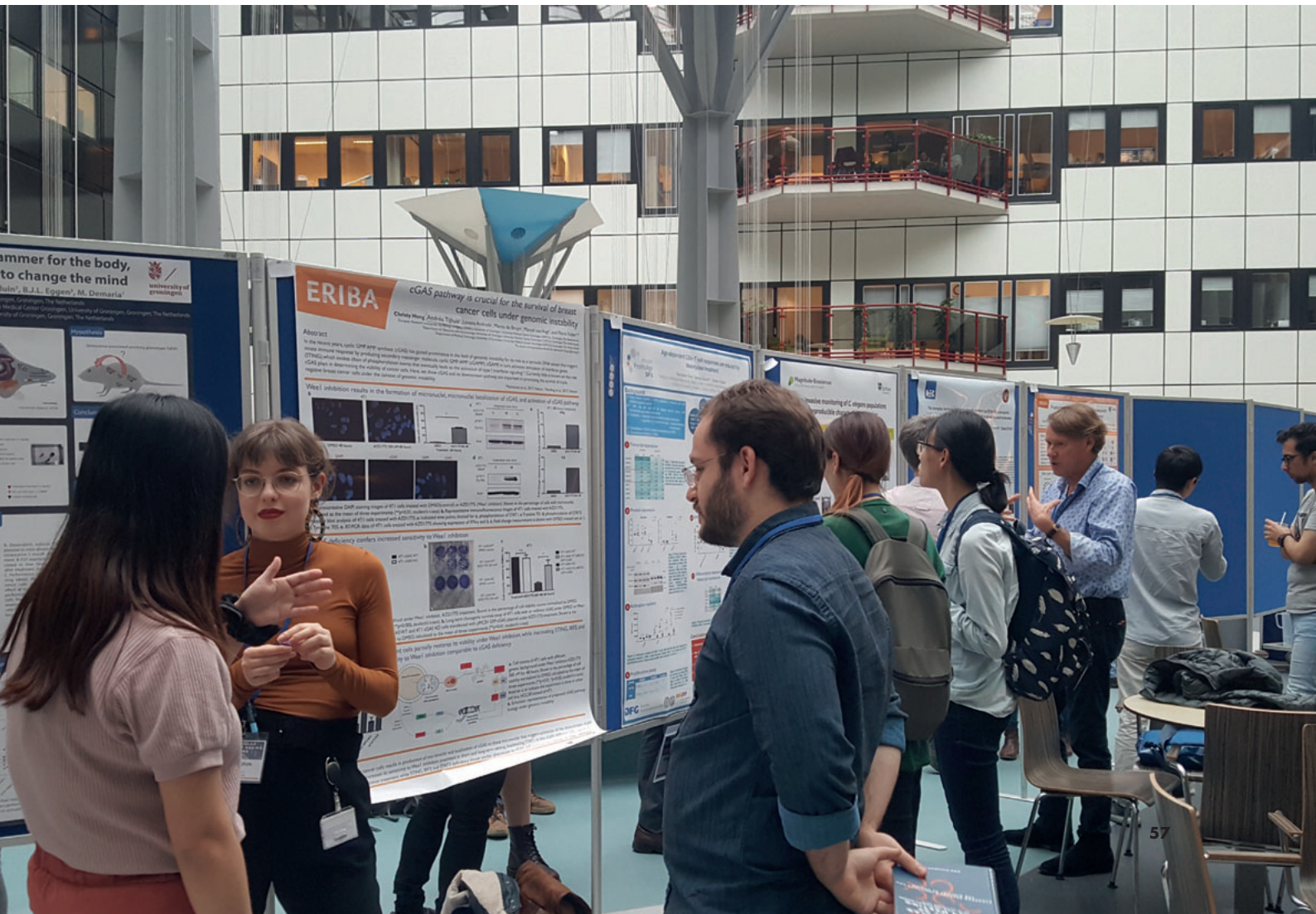
- ERIBA scientist Judith Paridaen and her lab members Katya Dvorianinova, Glòria Casas Gimeno, Nynke Oosterhof represented the institute in Science Fair 'University of Noorderzon' organized by the Young Academy Groningen. They had an exhibit on DNA at the event.
- Anton Steen, a member of Liesbeth Veenhoff's group also represented the institute at the event. He, in cooperation with Healthy Ageing Network Northern Netherlands (HANNN), organised Escape room, crack the code of happiness.
- Michael Chang presented about "model organisms in ageing research" at the Sum merschool Healthy Ageing.
- Liesbeth Veenhoff hosted professionals (directors and managers) from the public and private sectors following the 'Comenius Leergang' at ERIBA.
- Floris Foijer shared his expertise on CRISPR and aneuploidy to ex UMCG employees. He also organised and offered a tour on single cell sequencing for Care4BrittleBones. Additionally, he also presented at an event organised Chemische Kring Groningen-KCNV.
- At the Pint of Science event held in Groningen Jaskaren Kohli (a Postdoc in Demaria's group) and Mandy Koopman (PhD student in Ellen Nollen's lab) helped organize the event and also gave a seminar on their research. Floris Foijer also participated and pre sented in this event.
- Judith Paridaen was the Invited spreaker at Science Cafe Nijmegen "Genregulatie, het algoritme van het leven"
- Katya Dvorianinova, a member in Judith Paridaen's lab organised a work visit for high school students Willem Lodewijk Gymnasium Wetenschapstweedaagse".
- Leen Janssen and Renee Seinstra from Ellen Nollen's lab helped organise an activity for "student for a day" orientation event by University of Groningen.
- ERIBA hosted 30 TU Delft students for a lab tour on May 10th 2019

Science in a Box

Leading Staff member:
Stijn Mouton

In 2019, "Science in a Box" was officially launched, and the first "Regeneration Boxes" were sold. These Boxes provide a hands-on experience to explore topics as regeneration and stem cells in the class room. More information can be found on our website: scienceinabox.nl

During autumn, we started our online promotion which included a short video introduc- ing the concept. This video was actively shared on several online channels of ERIBA and the UMCG, and received a high number of views. In addition, interviews about the development of "Science in a Box" were given for Polsslag and Kennisinzicht.


ERIBA
cGAS pathway is crucial for the survival of breast cancer cells under genomic instability

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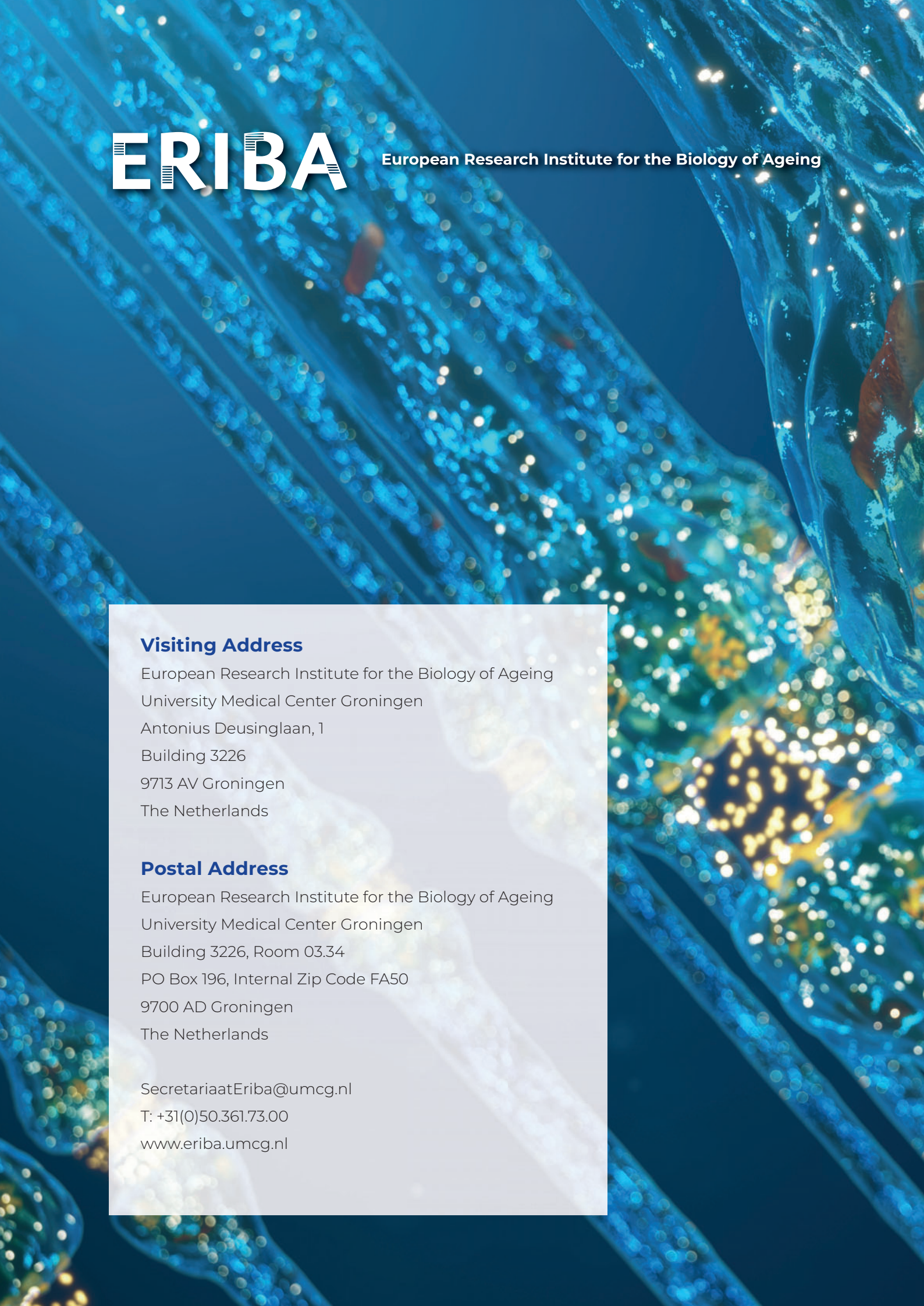

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