ERIBA

European Research Institute for the Biology of Ageing

Annual Report 2017

university of groningen

University Medical Center Groningen

Annual Report 2017

ERIBA

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Foreword
2017 in review

In 2017 ERIBA scientists secured a VIDI award and multiple grants from the Dutch Cancer Society. A former PhD student has been honoured with a Rubicon Fellowship, which we are very proud of.

I am very pleased to share with you the 2017 Annual Report of the European Research Institute for the Biology of Ageing. It has now been five years since our doors opened in 2012, and I am happy and proud to say that it has been a tremendous journey.

We built an Institute from scratch.

We recruited a wonderful team of scientists and staff and attracted promising students from many parts of the globe.

We established new national and international alliances and strengthened existing collaborations we want to pursue in the years to come.

We secured a significant amount of external funding through prestigious and highly competitive grants at national and European levels.

Again, a journey each of us should be proud of!

Early in 2017, we were for the first time evaluated by our Scientific Advisory Board (SAB), composed of internationally recognized scientists (see page 41) who were asked to conduct a thorough review of our first five years' performance. We were honoured with great enthusiasm and encouragement: we have been highly complimented with our overall achievements and received thoughtful indications where we should expand in terms of science, education and funding.

We invite you to revisit the 2012-2016 Report which contains a comprehensive description of ERIBA's research avenues and an extensive compilation of ongoing projects (see link below).

The current Report provides a summary of the 2017 activities we want to draw special attention to. A lot of good news: more excellent papers, more employees, more PhD students, more interns.

Furthermore, we successfully organized for the second time the Molecular Biology of Ageing Meeting, with the participation of a large number of well renowned scientists and young investigators from around the world. We re-ran for the fourth time the Massive Open Online Course "Why do we age", which attracted over 5.000 students.

In ERIBA, ~80% of our budget originates from extramural sources. Our collective challenge for the next year(s) will be to even further increase our funding, which would enable us to grow and pursue high-risk (and hopefully) ground-breaking studies.

Our mission remains solid and relevant as ever: how do we age? We believe that ERIBA scientists will continue to contribute to identify molecular interventions that allow the slowing down of different aspects of the ageing process.

Gerald de Haan
Scientific Director
January 2018

The 2012-2016 Report is available here:
http://eriba.umcg.nl/wp-content/uploads/2015/12/report-2012-2016.pdf

Ageing Research at ERIBA

Ageing Research at ERIBA

Ageing is the major risk factor for many diseases, including cancer, dementia and diabetes. The mission of scientists in ERIBA is to prolong health. To do so, we study how ageing occurs in cells, tissues, organs, and indeed, whole organisms. If we understand how ageing happens, we can develop approaches to intervene in the ageing process.

There is no tissue in our body that is immune to ageing. Nevertheless, exciting scientific discoveries have shown that it is very well possible to intervene in the ageing process. So, although ageing may be inevitable, it is also modifiable. This is also seen in humans; some people age fast, whereas other age much slower and remain healthy till advanced age.

While ageing is associated with many distinct diseases and affect all organs, we believe that molecularly ageing is caused by only a limited number of things that go wrong: “one cause, many problems”. Scientists in ERIBA therefore study the root cause of ageing, and find ways to intervene in them.

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

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 Calkoven 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 Michal 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.

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.

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.

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”.

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.

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.

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.

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.

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.

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.

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.

2017
A Closer Look

2017
A Closer Look

This section reports a selected number of achievements that have been accomplished within the various Laboratories of ERIBA throughout 2017.

Scientific Publications

In 2017 scientists in ERIBA published a record number of **55 papers** (see complete list in pages 20 to 25). More importantly, many of these papers resulted from joint collaborative research projects of various research groups within ERIBA, or from projects of ERIBA scientists with scientists in the University Medical Center Groningen. This testifies to the collaborative spirit which is essential in modern science.

It is great to see that the efforts that **Peter Lansdorp** and his group invested in single cell genetic analyses has come to full fruition and has led to multiple joint papers, with more to come. As an example, together with **Floris Foijer** and other collaborating labs they showed in a paper in Development Cell that centrosome amplification is sufficient to promote spontaneous tumour formation.

> Levine MS, Bakker B, Boeckx B, Moyett J, Lu J, Vitre B, Spierings DC, Lansdorp PM, Cleveland DW, Lambrechts D, Foijer F, Holland AJ. *Centrosome Amplification Is Sufficient to Promote Spontaneous Tumorigenesis in Mammals.* Dev Cell. 2017 Feb 6;40(3):313-322.e5

Gerald de Haan and **Seka Lazare**, his PhD student, wrote an authorative review on hematopoietic stem cell aging for BLOOD, the prime journal in the field.

> de Haan G and Lazare S. *Aging of hematopoietic stem cells.* Blood 2017, in press

Eugene Berezikov's group has been successful in annotating the genome of their favorite model organism, *Macrostomum lignano,* (published in Nature Communications), and indeed has achieved transgenesis of this animal, which now allows for sophisticated in vivo genetic experiments.

> Wudarski J, Simanov D, Ustyantsev K, de Mulder K, Grelling M, Grudniewska M, Beltman F, Glazenburg L, Demircan T, Wunderer J, Qi W, Vizoso DB, Weissert PM, Olivieri D, Mouton S, Guryev V, Aboobaker A, Schärer L, Ladurner P & Berezikov E. (2017). *Efficient transgenesis and annotated genome sequence of the regenerative flatworm model Macrostomum lignano.* "Nat Commun. 2017 Dec 14;8(1):2120.

The lab of **Cor Calkhoven** published a paper in Cell Reports, in which they identify the transcription factor C/EBPα as a key mediator of energy homeostasis. In addition, Cor's lab published a paper which describes a screening strategy to identify drugs that may classify as calorie restriction mimetics and have anti-cancer effects.

> Zaini, M.A., Müller, C., de Jong, T., Ackermann, T., Hartleben, G., Kortman, G., Gührs, K-H., Fusetti, F., Krämer, O.H., Guryev, V. and Calkhoven, C.F. (2017). *A p300 and SIRT1 regulated acetylation switch of C/EBPα controls mitochondrial function.* Cell Reports, accepted.

> Zaini, M.A., Müller, C., Ackermann, T., Reinshagen, J., Kortman, G., Pless, O., Calkhoven, C.F. (2017). *A screening strategy for the discovery of drugs that reduce C/EBPβ-LIP translation with potential calorie restriction mimetic properties.* Scientific Rep. 7:42603.

Michael Chang's group published a paper in which they determine what the minimal end of a telomere is and how the ends of chromosomes are recognized differently than DNA breaks. In addition, his group collaborated with **Peter Lansdorp**'s and Victor Guryev to develop a method to employ Strand-Seq in yeast (published in eLife).

Claussin, C., Porubsk , Spierings, D.C.J., Halsema, N., Rentas, S., Guryev, V., Lansdorp, P.M.*, and Chang, M.* *Genome-wide mapping of sister chromatid exchange events in single yeast cells using Strand-seq*. elife, in press.
*Co-corresponding author

Marco Demaria's team identified transcriptome signatures associated with specific senescent cell types and showed that the senescent phenotype is dynamic, changing at varying intervals after senescence induction. These novel transcriptome signatures, published in Current Biology, may help to discriminate among diverse senescence programs, but also as the basis for developing drugs specifically interfering with sub-types of senescent cells.

Hernandez-Segura A, de Jong TV, Melov S, Guryev V, Campisi J, Demaria M *Unmasking Transcriptional Heterogeneity in Senescent Cells*. Curr Biol. 2017 Sep 11;27(17):2652-2660.e4.

Ellen Nollen's group, together with **Cor Calkhoven** and **Victor Guryev**, published a paper in Molecular Cell in which they identify a novel, small non-coding RNA-mediated mechanism that is involved in disease-associated protein aggregation.

Sin O, de Jong T, Kudron M , Zaini A , Aprile F.A , Seinstra R, Mata-Cabana A, Stroo E, Willinge Prins R, Martineau C, Wang H.H, Hogewerf W, Steinhof A, Wanker E.E, Vendruscolo M, Calkhoven C.F, Reinke V, Guryev V, Nollen E.A.A. *Identification of an RNA Pol III-associated regulator of small non-coding RNAs that is linked with disease-associated protein aggregation*. Mol Cell. 2017 Mar 16;65(6):1096-1108.e6.

Liesbeth Veenhoff wrote a book chapter on how to use a combination of computational methods and in vivo measurements of transport kinetics in wild type, mutant and aged nuclear pore complexes to understand how the NPCs are selective gates.

Grants

ERIBA scientists secured external funding, totalling **3,1 M Euro**. These grants included a VIDI and Aspasia award to Judith Paridaen, from the 'Nederlandse Organisatie voor Wetenschappelijk Onderzoek', three grants from the Dutch Cancer Society to Cor Calkhoven and Marco Demaria, and a grant from the Landsteiner Foundation for Blood Transfusion Research to Gerald de Haan. Detailed information can be found in page 26.

Awards

Several of ERIBA's students or postdocs won awards. **Johannes Jung** was awarded the New Investigator Prize at the 46th Annual Meeting of the International Society for Experimental Hematology in Frankfurt.

Weilin Liu, postdoctoral fellow shared between the labs of Gerald de Haan, Peter Lansdorp and Floris Foijer was awarded the Chinese Government Award for Outstanding Students Abroad. This prize was awarded to Weilin for his excellent PhD work in the lab of Hans Jonker at the University Medical Center Groningen that yielded publications in PNAS and Nature.

Olga Sin, a former PhD student at Nollen's group who graduated in 2016, was awarded a prestigious Rubicon grant by NWO. Olga has moved to the Max Planck Institute for Molecular Biomedicine, in Germany, where she will investigate how defective protein production is linked to neurodegeneration..

Georges Janssens, a former PhD student of the Veenhoff group who graduated in 2016, was awarded a FEBS long-term fellowship. After a first postdoc at former ERIBA PI Christian Riedel at the Karolinska Institute, he moved to the Houtkooper lab at the AMC Amsterdam, where he will continue his career studying modulators of ageing.

Anita Pras in Ellen Nollen's lab won this year's ERIBA Trainee Award.

Graduations

There were six students in ERIBA who successfully defended their PhD thesis, and have since moved on to their next position. These include **David Porubsky** (Lansdorp lab, currently at the Max Planck Institute for Informatics, Saarbrüken), **Magda Grudniewska-Lawton** (Berezikov lab, now at Rutgers University, New Jersey), **Mohammad Amr Zaini** (Calkhoven lab, now at VUmc, Amsterdam), **Clémence Claussin** (Chang lab, now at Sloan Kettering Institute, New York), **Hilda van den Bos** (Lansdorp lab, now a Postdoctoral Fellow in ERIBA) and **Helen Michels** (Nollen lab, now in Polycheck in Germany).

Scientific Dissemination and Public Outreach

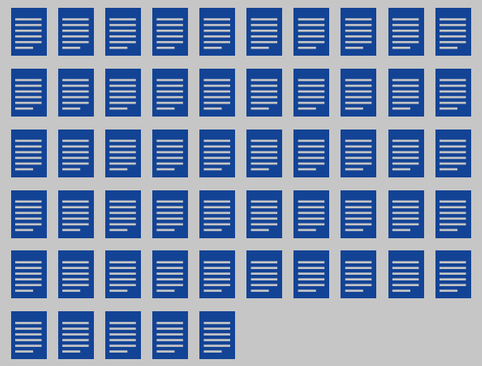
For the second time, ERIBA organised the Molecular Biology of Ageing Meeting in Groningen, and once more we succeed to gather world-leading scientists working in the diverse research areas that are relevant for understanding the biology of ageing and more than 200 participants attended this event (www.bioageing.nl). The third edition will happen in the Fall of 2019.

ERIBA's scientists were also involved in numerous outreach activities in which they aim to share their findings with society at large. In 2017 we hosted many visitors to our labs and participated in local Science Fairs. See pages 38 and 39 of this report for more information on outreach and dissemination activities.

Facts and Figures

Scientific Publications

NUMBER OF SCIENTIFIC PUBLICATIONS IN 2017



2017

55

2011 · 12
2012 · 22
2013 · 37
2014 · 34
2015 · 39
2016 · 40

Publications per Research Group

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

1. **Wudarski J**, Simanov D, Ustyantsev K, de Mulder K, **Grelling M, Grudniewska M, Beltman F, Glazenburg L**, Demircan T, Wunderer J, Qi W, Vizoso DB, Weissert PM, Olivieri D, Mouton S, Guryev V, Aboobaker A, Schärer L, Ladurner P, **Berezikov E**. Efficient transgenesis and annotated genome sequence of the regenerative flatworm model Macrostomum lignano. Nat Commun. 2017 Dec 14;8(1):2120.

2. van der Pol A, Gil A, Silljé HHW, Tromp J, **Ovchinnikova ES**, Vreeswijk-Baudoin I, Hoes M, Domian IJ, van de Sluis B, van Deursen JM, Voors AA, van Veldhuisen DJ, van Gilst WH, **Berezikov E**, van der Harst P, de Boer RA, Bischoff R, van der Meer P. Accumulation of 5-oxoproline in myocardial dysfunction and the protective effects of OPLAH. Sci Transl Med. 2017 Nov 8;9(415). pii: eaam8574.

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5. **Hoffmann RF**, Moshkin YM, **Mouton S**, Grzeschik NA, Kalicharan RD, Kuipers J, Wolters AHG, Nishida K, Romashchenko AV, Postberg J, Lipps H, **Berezikov E**, Sibon OCM, Giepmans BNG, **Lansdorp PM**. Guanine quadruplex structures localize to heterochromatin. Nucleic Acids Res. 2017 Jun 2;45(10):6253.

6. Vegter EL, **Ovchinnikova ES**, Silljé HHW, Meems LMG, van der Pol A, van der Velde AR, **Berezikov E**, Voors AA, de Boer RA, van der Meer P. Rodent heart failure models do not reflect the human circulating microRNA signature in heart failure. PLoS One. 2017 May 5;12(5):e0177242.

7. Vegter EL, **Ovchinnikova ES**, van Veldhuisen DJ, Jaarsma T, **Berezikov E**, van der Meer P, Voors AA. Low circulating microRNA levels in heart failure patients are associated with atherosclerotic disease and cardiovascular-related rehospitalizations. Clin Res Cardiol. 2017 Aug;106(8):598-609.

Laboratory of Gene Regulation In Ageing and Age-Related Diseases
Group Leader: Cor Calkhoven

1. **Zaini, M.A.**, Müller, C., de Jong, T., **Ackermann, T.**, Hartleben, G., Kortman, G., Gührs, K-H., Fusetti, F., Krämer, O.H., **Guryev, V.** and **Calkhoven, C.F.** (2017). A p300 and SIRT1 regulated acetylation switch of C/EBPα controls mitochondrial function. Cell Reports, accepted

2. Hu D, Essig K, Guimaraes J.C., Alterauge D, Edelmann S, Heiseke A, Floess S, Klein J, Maiser A, Marschall S, Hrabě de Angelis, M, Leonhardt H, **Calkhoven C.F**, Huehn J, Krug A, Baumjohann D, Zavolan M and Heissmeyer V. Roquin suppresses PI3K-mTOR signaling to control protein biosynthesis, T cell differentiation and Treg effector function. Immunity. 47, 1067–1082 December 19, accepted.

3. **Sin O**, de Jong T, Kudron M, **Zaini A**, Aprile F.A, **Seinstra R**, **Mata-Cabana A**, **Stroo** E, Willinge Prins R, **Martineau C**, Wang H.H, **Hogewerf W**, Steinhof A, Wanker E.E, Vendruscolo M, **Calkhoven C**.F, Reinke V, **Guryev V**, **Nollen E.A.A.** Identification of an RNA Pol III associated regulator of small non-coding RNAs that is linked with disease-associated protein aggregation. Mol Cell. 2017 Mar 16;65(6):1096-1108.e6.

4. **Zaini MA, Müller C, Ackermann T**, Reinshagen J, **Kortman G**, Pless O, **Calkhoven CF** (2017). A screening strategy for the discovery of drugs that reduce C/EBPβ-LIP translation with potential calorie restriction mimetic properties. Sci Rep. 2017 Feb 15;7:42603.

Laboratory of Telomeres and Genome Integrity
Group Leader: Michael Chang

1. **Claussin C, Porubsk D, Spierings DCJ, Halsema N**, Rentas S, **Guryev V**, **Lansdorp PM***, **Chang M***. Genome-wide mapping of sister chromatid exchange events in single yeast cells using Strand-seq. eLife Dec.12 2017;6:e30560. *Co-corresponding author

2. **Stinus S, Paeschke K, Chang M**. Telomerase regulation by the Pif1 helicase: a length-dependent effect? Curr Genet. 2017 Oct 20.

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6. **Cabrera M, Novarina D, Rempel IL, Veenhoff LM, and Chang M**. A simple microfluidic platform to study age-dependent protein abundance and localization changes in *Saccharomyces cerevisiae*. Microb Cell. 2017 Apr 13;4(5):169-174.

Laboratory of Quantitative Epigenetics
Group Leader: Maria Colomé Tatché

1. Kebede AF, Nieborak A, Shahidian LZ, Le Gras S, Richter F, Gómez D, Baltissen MP, Meszaros G, Magliarelli HF, **Taudt A**, Margueron R, **Colomé-Tatché M**, Ricci R, Daujat S, Vermeulen M, Mittler G, Schneider R. Histone propionylation is a mark of active chromatin. Nat Struct Mol Biol. 2017 Dec;24(12):1048-10

2. Richards CL, Alonso C, Becker C, Bossdorf O, Bucher E, **Colomé-Tatché M**, Durka W, Engelhardt J, Gaspar B, Gogol-Döring A, Grosse I, van Gurp TP, Heer K, Kronholm I, Lampei C, Latzel V, Mirouze M, Opgenoorth L, Paun O, Prohaska SJ, Rensing SA, Stadler PF, Trucchi E, Ullrich K, Verhoeven KJF. Ecological plant epigenetics: Evidence from model and non-model species, and the way forward. Ecol Lett. 2017 Dec;20(12):1576-159056

3. Ferronika P, **van den Bos H, Taudt A, Spierings DCJ**, Saber A, Hiltermann TJN, Kok K, **Porubsky D**, van der Wekken AJ, Timens W, **Foijer F**, **Colomé-Tatché M**, Groen HJM, **Lansdorp PM**, van den Berg A. Copy number alterations assessed at the single-cell level revealed mono- and polyclonal seeding patterns of distant metastasis in a small-cell lung cancer patient. Ann Oncol. 2017 Jul 1;28(7):1668-1670.

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

1. **Belderbos ME, Bystrykh L, de Haan G**, Left or right? Directions to stem cell engraftment. J Exp Med. 2017 Nov 28. pii: jem.20171904.

2. **De Haan G** and **Lazare S.** Aging of hematopoietic stem cells. Blood. 2017 Nov 15. pii: blood-2017-06-746412.

3. Martín-Pardillos A, Tsaalbi-Shtylik A, Chen S, **Lazare S**, **van Os RP**, **Dethmers-Ausema A**, Fakouri NB, Bosshard M, Aprigliano R, van Loon B, Salvatori DCF, Hashimoto K, Dingemanse-van der Spek C, Moriya M, Rasmussen LJ, **de Haan G**, Raaijmakers MHGP, de Wind N. Genomic and functional integrity of the hematopoietic system requires tolerance of oxidative DNA lesions. Blood. 2017 Sep 28;130(13):1523-1534.

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6. **Jung JJ, Buisman SC, de Haan G**. Do hematopoietic stem cells get old? Leukemia. 2017 Mar;31(3):529-531.

Laboratory of Cellular senescence and age-related pathologies
Group Leader: Marco Demaria

1. **Hernandez-Segura A, de Jong TV, Guryev V**, Campisi J, **Demaria M**. Unravelling transcriptional heterogeneity of senescent cells. Curr Biol. 2017 Sep 11;27(17):2652-2660.e4.

2. Jeon Oh, Kim C, Laberge RM, **Demaria M**, Rathod S, Vasserot A, Chung JW, Kim DH, Poon Y, David N, Baker DJ, Van Deursen JM, Campisi J, Elisseeff JH. Clearance of senescent cells prevents the development of post-traumatic osteoarthritis and creates a pro-regenerative environment. Nat Med. 2017 Jun;23(6):775-781.

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

1. **Schukken KM**, **Foijer F**, CIN and Aneuploidy: Different Concepts, Different Consequences. Bioessays. 2017 Nov 21.

2. **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. 2017 Sep 23. pii: S1357-2725(17)30249-2.

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4. Ferronika P, **van den Bos H, Taudt A, Spierings DCJ**, Saber A, Hiltermann TJN, Kok K, **Porubsky D**, van der Wekken AJ, Timens W, **Foijer F, Colomé-Tatché M**, Groen HJM, **Lansdorp PM**, van den Berg A. Copy number alterations assessed at the single-cell level revealed mono- and polyclonal seeding patterns of distant metastasis in a small-cell lung cancer patient. Ann Oncol. 2017 Jul 1;28(7):1668-1670.

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6. Soto M, Raaijmakers JA, **Bakker B, Spierings DCJ, Lansdorp PM, Foijer F**, Medema RH. p53 Prohibits Propagation of Chromosome Segregation Errors that Produce Structural Aneuploidies. Cell Rep. 2017 Jun 20;19(12):2423-2431.

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8. Levine MS, Bakker B, Boeckx B, Moyett J, Lu J, Vitre B, **Spierings DC, Lansdorp PM**, Cleveland DW, Lambrechts D, **Foijer F**, Holland AJ. Centrosome Amplification Is Sufficient to Promote Spontaneous Tumorigenesis in Mammals. Dev Cell. 2017 Feb 6;40(3):313-322.e5

9. **Van den Bos H, Spierings DCJ, Foijer F, Lansdorp PM.** Does aneuploidy in the brain play a role in neuro-degenerative disease? Book chapter in 'Chromosomal Abnormalities – A Hallmark Manifestation of Genomic Instability', InTech Aug. 30, 2017.

Laboratory of Genome Structure Ageing
Group Leader: Victor Guryev

1. **Claussin C, Porubsk D, Spierings DCJ, Halsema N**, Rentas S, **Guryev V, Lansdorp PM, Chang M**. Genome-wide mapping of sister chromatid exchange events in single yeast cells using Strand-seq, eLife Dec.12 2017;6:e30560.

2. **Porubsky D**, Garg S, Sanders AD, Korbel JO, **Guryev V**, **Lansdorp PM**, Marschall T. Dense and accurate whole-chromosome haplotyping of individual genomes. Nat Commun. 2017 Nov 3;8(1):1293.

3. Mahmud H, Scherpen FJG, de Boer TM, Lourens HJ, Schoenherr C, Eder M, Scherr M, **Guryev V**, De Bont ES. Peptide microarray profiling identifies phospho-lipase C gamma 1 (PLC-γ1) as a potential target for t(8;21) AML. Oncotarget. 2017 Jun 27;8(40):67344-67354.

4. **Hernandez-Segura A**, **de Jong TV**, Melov S, **Guryev V**, Campisi J, **Demaria M**. Unmasking Transcriptional Heterogeneity in Senescent Cells. Curr Biol. 2017 Sep 11;27(17):2652-2660.e4.

5. **Van Wietmarschen N**, **Merzouk S**, **Halsema N**, **Spierings DCJ**, **Guryev V**, **Lansdorp PM**. BLM helicase suppresses recombination at G-quadruplex motifs in transcribed genes. bioRxiv 2017 August 7 3252.

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Laboratory of Genetic Instability and Ageing
Group Leader: Peter Lansdorp

1. **Porubsk D**, **Spierings DCJ**, **Halsema N**, Rentas S, **Guryev V**, **Lansdorp PM**, **Clémence Claussin**, **Chang M** Co-corresponding author. Genome-wide mapping of sister chromatid exchange events in single yeast cells using Strand-seq, eLife Dec.12 2017;6:e30560

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Laboratory of Molecular Neurobiology of Ageing
Group Leader: Ellen Nollen

1. Yoshimura Y, Holmberg MA, Kukic P, Andersen CB, **Mata-Cabana A**, Falsone SF, Vendruscolo M, **Nollen EAA**, Mulder FAA. MOAG-4 promotes the aggregation of -synuclein by competing with self-protective electrostatic interactions. J Biol Chem. 2017 May 19;292(20):8269-8278.

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Laboratory of Nucleic Acids Structures and Repair
Group Leader: Katrin Paeschke

1. **Schwindt E**, **Paeschke K**. Mms1 is an assistant for regulating G-quadruplex DNA structures. Curr Genet. 2017 Nov 2.

2. **Stinus S**, **Paeschke K**, **Chang M**. Telomerase regulation by the Pif1 helicase: a length-dependent effect? Curr Genet. 2017 Oct 20.

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5. **Kazemier HG**, **Paeschke K**, **Lansdorp PM**. Guanine quadruplex monoclonal antibody 1H6 cross-reacts with restrained thymidine-rich single stranded DNA. Nucleic Acids Res. 2017 Jun 2;45(10):5913-5919.

6. Benhalevy D, Sanjay K. Gupta, Danan CH, Ghosal S, Sun3 HW, **Kazemier H.G.**, **Paeschke K**, Hafner M, **Juranek SA**. The Human CCHC-type Zinc Finger Nucleic Acid-Binding Protein Binds G-Rich Elements in Target mRNA Coding Sequences and Promotes Translation. Cell Rep. 2017 Mar 21;18(12):2979-2990.

Laboratory of Cellular Biochemistry
Group Leader: Liesbeth Veenhoff

1. Ghavami A, **Veenhoff LM**, van der Giessen E and Onck P.R. Coarse-grained molecular dynamics of the natively-unfolded domain of the NPC. in Nuclear-Cytoplasmic Transport; NAMB, Springer (2017)

2. **Novarina D**, **Mavrova SN**, **Janssens GE**, **Rempel IL**, **Veenhoff LM**, **Chang M**. Increased genome instability is not accompanied by sensitivity to DNA damaging agents in aged yeast cells. DNA Repair (Amst). 2017 Jun;54:1-7.

3. **Cabrera M**, **Novarina D**, **Rempel IL**, **Veenhoff LM**, and **Chang M**. A simple microfluidic platform to study age-dependent protein abundance and localization changes in Saccharomyces cerevisiae. Microb Cell. 2017 Apr 13;4(5):169-174.

Funding/Grants

Funding (Awarded Grants)

2017

€ 3,1 M

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

Research proposals awarded in 2017

Principal Investigator	Role	Grant	Title	Budget
Judith Paridaen	Applicant	VIDI / NWO	The individuality of stem cells	€ 800.000
	Applicant	Aspasia / NWO	---	€ 100.000
Klaske Schukken	Applicant	de Cock	Een muismodel om aneuploïdie en missegregatie in vivo te visualiseren	€ 4.000
Anita Pras	Applicant	de Cock	De endogene functie van de amyloid regulerende factor SERF2 in embryonale ontwikkeling	€ 4.000
Mandy Koopman	Applicant	de Cock	Het identificeren van genen en bijbehorende genetische netwerken die toxiciteit van TARDP-43 (TDP-43) moduleren	€ 4.000
Floris Foijer	Applicant	KACST	The effect of age on iPSc reprogramming efficiency and differentiation potential	€ 132.000
Cor Calkhoven	Applicant	KWF	Modulation of the TSC-mTORC1-mitochondrial pathway for suppression of MYC-driven tumourgenesis	€ 647.459
Marco Demaria	Applicant	KWF	Characterization of UV-induced senescent cells during melanoma progression	€ 615.475
	Co-applicant	KWF	Senescence Early after Chemotherapy for testicular cancer treatment: Time to act (SAE-CAT)	€ 373.066
Gerald de Haan	Applicant	LSBR	Dissecting the role of Neogenin; a novel receptor required for hematopoietic stem cell proliferation and engraftment	€ 438.254

NOW – Netherlands Organisation for Scientific Research
de Cock – Jan Kornelis de Cock Stichting
KACST – King Abdulaziz City for Science and Technology
KWF – Dutch Cancer Society
LSBR – Landsteiner Foundation for Blood Transfusion Research

Invited Speakers

During 2017, many prominent scientists have been invited to give talks and lectures in the premises of ERIBA and the University Medical Center Groningen.

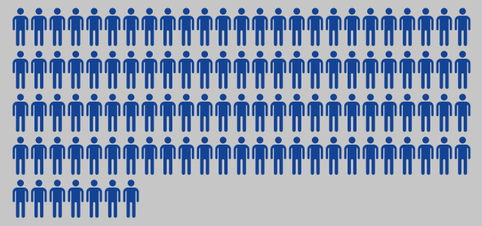
Speakers	Host	Title of Talk/Lecture	University/Institute	Event
Claudio Hetz	Jon Laman en Floris Foijer	Proteostasis imbalance and neurodegenerative diseases	Biomedical Neuroscience Institute (BNI), Faculty of Medicine, University of Chile, Santiago, Chile and Harvard School of Public Health, Boston, USA	Molecular Medicine Series
Caroline Kisker	Katrin Paschke	The role of the two helicases XPD and RecQ4 in genome maintenance	Rudolf Virchow Center for experimental Biomedicine, Julius Maximilians University, Würzburg, Germany	Molecular Medicine Series
Michele Vendruscolo	Ellen Nollen	Systematic development of small molecules against Abeta aggregation in Alzheimer's disease	Dept. of Chemistry, University of Cambridge, Cambridge, UK	Molecular Medicine Series
Jan Tuckermann	Cor Calkhoven	Glucocorticoid receptor action in Osteoimmunology and novel regulators in bone integrity	Institute of Comparative molecular endocrinology, University of Ulm, Germany	Molecular Medicine Series
Helle Ulrich	Katrin Paescke	Dealing with DNA damage during replication	Institute of Molecular Biology (IMB), Mainz, Germany	Molecular Medicine Series
Collin Y Ewald	Marco Demari	Prolonged extracellular matrix homeostasis is essential for healthy aging	ETH Zürich, Switzerland	Molecular Medicine Series
Rik Korswagen	Eugene Berezikov	Cell intrinsic modulation of wnt signaling as a guidance mechanism in neuroblas migration	Hubrecht Institute, Utrecht	Molecular Medicine Series
Daniel Durocher	Michael Chang	Charting the response to DNA damage with CRISPR screens	Samuel Lunenfeld Research Institute,University of Toronto,Canada	Molecular Medicine Series
Valeria Poli	Marco Demaria	One, no one, one hundred thousand: the many fae of the transcription factor STAT3 in cancer and autoimmunity	Molecular bio-technology Center, University of Turin, Italy	Molecular Medicine Series
Stefano Biffo	Cor Calkhoven	Translational control of metabolism	University of Milano, Italy	Friday Meetings
Andrew Dillin	Ageing Meeting	The communication of Mitochondrial Protetoxic Stress (the Mitokine	Department of molecular and Cell Biology at Berkeley, USA	Molecular Biology of AgeingMeeting
Joachim Lingner	Ageing Meeting	Telomeric chromatin analysis provides insights into damage protection	École Polytechnique Fédérale de Lausanne	Molecular Biology of AgeingMeeting
Jan Karlseder	Ageing Meeting	Regulation of DNA Repair pathway choice in S/G2 by the NHEJ inhibitor CYREN	Salk Institute for Biological Studies	Molecular Biology of AgeingMeeting
Miguel Godinho Ferreira	Ageing Meeting	Non-cell autonomous effects of telomere shortening in cancer and ageing	Institute for Research on Cancer and Aging in Nice (IRCAN	Molecular Biology of AgeingMeeting
Peter Baumann	Ageing Meeting	Telomerase RNA biogenesis – it takes a lot to make enough	HHMI and Stowers Institute, Kansas University Medical Center	Molecular Biology of AgeingMeeting
Jan Hoeijmakers	Ageing Meeting	Keeping your genome intact protects you from aging and neurodegeneration	Erasmus MC Department of Molecular Genetics	Molecular Biology of AgeingMeeting
Penny Jeggo	Ageing Meeting	Maintaining Genomic Integrity in the face of DNA double strand breaks	School of Life Sciences at the University of Sussex	Molecular Biology of AgeingMeeting
Anne Cornelis Meinema	Ageing Meeting	DNA circles cause nuclear pore complex rearrangements during yeast aging	ETH Zürich	Molecular Biology of AgeingMeeting
Jacqueline Jacobs	Ageing Meeting	Control of DNA repair path-way choice at telomeres and DNA double strand breaks	The Netherlands Cancer Institute	Molecular Biology of AgeingMeeting
Elsa Logarinho	Ageing Meeting	Molecular basis of mitotic decline during human aging	IBMC-Instituto de Biologia Molecular e Celular, i3S, Porto University	Molecular Biology of AgeingMeeting
Liza Pon	Ageing Meeting	Reciprocal interactions between mitochondrial DNA and lifespan control in budding yeast	Columbia University Medical Center	Molecular Biology of AgeingMeeting
Marte Molenaars	Ageing Meeting	The Interplay between Mitochondrial Function and Protein Translation in Longevity	Academic Medical Center Amsterdam	Molecular Biology of AgeingMeeting
Vincenzo Sorrentino	Ageing Meeting	Enhancing mitochondrial proteostasis reduces amyloid-ß peptide proteotoxicity	École Polytechnique Fédérale de Lausanne	Molecular Biology of AgeingMeeting
Jens Bruening	Ageing Meeting	Neuronal circuits in control of metabolism	Max Planck Institute for Metabolism Research	Molecular Biology of AgeingMeeting
Brian Kennedy	Ageing Meeting	Sex Differences and Aging in the mTOR Pathway	The Buck Institute for Research on Aging	Molecular Biology of AgeingMeeting
Christine Müller	Ageing Meeting	Reduced expression of C/ EBPß-LIP extends health- and lifespan in mice	European Research Institute for the Biology of Ageing, UMCG	Molecular Biology of AgeingMeeting

Speakers	Host	Title of Talk/Lecture	University/Institute	Event
Peter Tessarz	Ageing Meeting	Integration of metabolic and epigenetic regulation of stem cell fates in health and ageing	Max Planck Institute for Biology of Ageing, Cologne	Molecular Biology of AgeingMeeting
David Rubinsztein	Ageing Meeting	Autophagy and Neurodegeneration	Cambridge Institute for Medical Research	Molecular Biology of AgeingMeeting
Katja Simon	Ageing Meeting	Autophagy and immune aging	Oxford University	Molecular Biology of AgeingMeeting
Andre Nussenzweig	Ageing Meeting	Genome Organization Drives Chromosome Fragility	Center for Cancer Research, NIH	Molecular Biology of AgeingMeeting
Manolis Pasparakis	Ageing Meeting	Necroptosis in tissue homeostasis and inflammation	Institute for Genetics at the University of Cologne	Molecular Biology of AgeingMeeting
Edwin Cuppen	Ageing Meeting	Tissue-specific mutation accumulation in human adult stem cells during life	Center for Molecular Medicine at the UMC Utrecht	Molecular Biology of AgeingMeeting
Anne Brunet	Ageing Meeting	Understanding and modeling aging	Paul F. Glenn Laboratories for the Biology of Aging at Stanford University	Molecular Biology of AgeingMeeting
Mario Baumgart	Ageing Meeting	Longitudinal analysis of gene expression in the short-lived killifish Nothobranchius furzeri reveals widespread pleiotropic antagonistic actions	Leibniz Institute on Aging - FLI	Molecular Biology of AgeingMeeting
Bart Eggen	Ageing Meeting	Transcriptomic analysis of purified human cortical microglia reveals age-associated changes	University Medical Center Groningen	Molecular Biology of AgeingMeeting
Markus Schosserer	Ageing Meeting	Two distinct ribosomal RNA base methylations modulate healthy lifespan	University of Natural Resources and Life Sciences, Vienna	Molecular Biology of AgeingMeeting
Mark S. Hipp	Ageing Meeting	Proteostasis impairment in protein misfolding and aggregation diseases	Max Planck Institute of Biochemistry	Molecular Biology of AgeingMeeting
Alessandro Cellerino	Ageing Meeting	Proteomic analysis of brain aging reveals reduction of protein/transcript correlation, loss of stoichiometry in multiple protein complexes and changes in protein thermal stability	Scuola Normale Superiore	Molecular Biology of AgeingMeeting
Tobias Dansen	Ageing Meeting	Proteome-wide Changes in Protein Turnover Rates in C. elegans Models of Longevity and Age-Related Disease	UMC Utrecht	Molecular Biology of AgeingMeeting

Speakers	Host	Title of Talk/Lecture	University/Institute	Event
Giovanna Mallucci	Ageing Meeting	Manipulating the Unfolded Protein Response for treatment of neurodegeneration	Department of Clinical Neurosciences, University of Cambridge	Molecular Biology of AgeingMeeting
Collin Ewald	Ageing Meeting	Preferential translation of ATF-5 mediates Caenorhabditis elegans lifespan extension from reduced protein synthesis	ETH Zurich	Molecular Biology of AgeingMeeting
Thomas Rando	Ageing Meeting	Epigenetics Mechanism of stem cell aging and rejuvenation	Glenn Center for the Biology of Ageing at Stanford University	Molecular Biology of AgeingMeeting
Allison Bardin	Ageing Meeting	Modes of genome alteration of adult stem cell during aging	Genetics and Developmental Biology Center at Institut Curie	Molecular Biology of AgeingMeeting
Allesandro Ori	Ageing Meeting	Age and diet affect the intestinal crypt proteome	Leibniz Institute on Aging – Fritz Lipmann Institute (FLI)	Molecular Biology of AgeingMeeting
Manuel Serrano	Ageing Meeting	Integrating cellular senescence and reprogramming	Institute for Research in Biomedicine, IRB Barcelona	Molecular Biology of AgeingMeeting
Sheila A. Stewart	Ageing Meeting	Age-related changes in the tumor microenvironment drive tumorigenesis	Department of Cell Biology and Physiology at the Washington University of St. Louis	Molecular Biology of AgeingMeeting
Peter de Keizer	Ageing Meeting	Targeted Apoptosis of Senescent Cells Restores Tissue Homeostasis in Response to Chemotoxicity and Aging	Department of Genetics, Erasmus MC Rotterdam	Molecular Biology of AgeingMeeting
Peter Bruno	Ageing Meeting	Functional genetic characterization of senescence induction	Harvard Medical School	Molecular Biology of AgeingMeeting
Sélène Glück	Ageing Meeting	Innate immune sensing of cytosolic chromatin fragments through cGAS promotes senescence	École Polytechnique Fédérale de Lausanne	Molecular Biology of AgeingMeeting
Peter Lansdorp	Diana Spierings	Structural genomic variation and instability	European Research Institute/ Terry Fox laboratory Canada	Molecular Medicine Series
Jan Dumanski	Floris Foijer	46XY minus Y+higher mortality and increased risk of cnacer as well as Alzheimer's disease in aging males	Dept. of Medical Genetics and Genomics,Uppsala University, Sweden	Molecular Medicine Series
John Diffley	Katrin Paeschke	How our genomes are copied	Francis Crick Institute, Londen, UK	Molecular Medicine Series
Luigi Fontana	Marco Demaria	Nutritional modulation of ageing and age-associated diseases	Università di Brescia,Italy & Washington University, USA	Molecular Medicine Series

People

EMPLOYEES

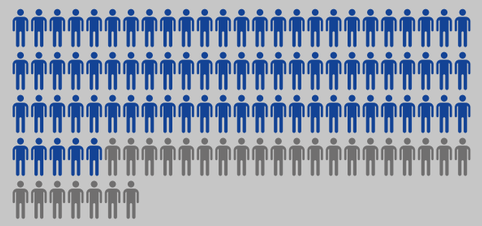


2017

107

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

STAFF UNDER 40 (%)

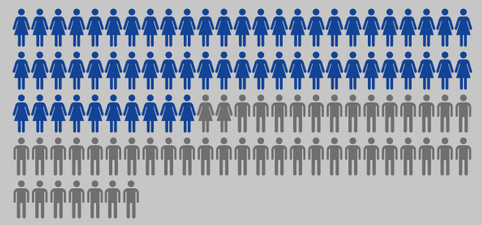


2017

76%

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

FEMALE EMPLOYEES (%)

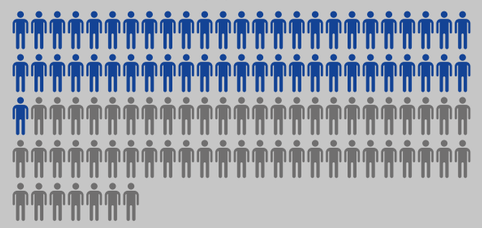


2017

54%

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

INTERNATIONALS (%)



2017

49%

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

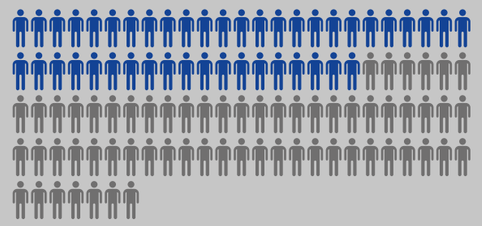
NUMBER OF NATIONALITIES

2017

23

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

DOCTORAL STUDENTS HOSTED BY ERIBA [1,2]



2017

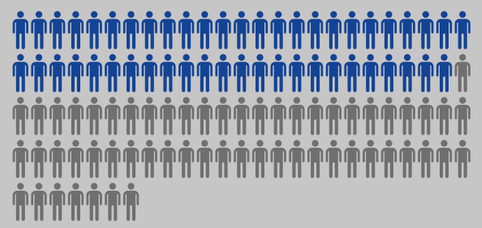
44

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

1 10 of these students are hosted by ERIBA under the GSMS Bursary Scheme, which was introduced by the Graduate School of Medical Sciences (GSMS) in 2017

2 6 of these students have defended their thesis in the course of 2017

INTERNS [3]



2017

49

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

3 Students who made internships in various labs

Education

Outreach and Dissemination

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.

"Model organisms in Ageing Research"
3 ECTS BSc Junior Scientific Master course, 11 students
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 'life of a basic biologist'.

"Current Themes in Healthy Ageing"
5 ECTS MSc course, 33 students
Coordinator: 2016-'17: **Floris Foijer**,
2017-'18: **Marco Demaria/Judith Paridaen**
Objectives: How to get most out of scientific seminars. Biomedical Science students attend 7- scientific seminars and verbally report on content, scientific excellence and track records of the presenters. Course has been growing rapidly and now has > 30 students/year.

"Genomics data analysis for biologists"
1,5 EC GSMS course, 20 PhD students from GSMS
September 2017 - January 2018: Weekly seminars
Coordinators: **Victor Guryev, Leonid Bystrykh**
Objectives: Discuss data analysis and educate ERIBA BSc, MSc and PhD students on genome biology tools.

"Molecular Biology of Ageing and Age related Disease"
5 ECTS MSc course, 34 biomedical students
November 2017
Coordinator: **Liesbeth Veenhoff**
Objectives: In this course we focus on the molecular and cellular mechanisms by which tissue and organ function deteriorate and homeostasis fails, resulting in ageing and age related disease. We present the model systems and experimental strategies that are used in ageing research. This course will be supported by a team of specialists in different fields of ageing that will provide lectures and reading material. The course will be further supported by materials from an online course "Why do we age? The molecular mechanisms of ageing". The course not only gives an overview of the research field of ageing but also teaches scientific writing, active listening and giving feedback to peers. The course unit is compulsory for the ageing track and is an elective in the other tracks of the programs.

"Mol. Biol. of Ageing and Age-related disease"
PhD level course, 13 students
November - December 2017
Coordinator: **Liesbeth Veenhoff, Marco Demaria**
Objectives: To provide PhD-students an overview of the current state of our knowledge of the molecular mechanisms underlying ageing and to train academic thinking and discussion. This course will be supported by ERIBA team leaders that will provide lectures and reading materials.

"BCN N-track", research master, 8 students
1 January - 31 December 2017
Coordinator: **Liesbeth Veenhoff**
Objectives: I act as the coordinator of this track specialized in molecular mechanisms of brain pathologies.

"Protein chemistry and proteomics methods" and **"Model Organisms"** master level course, top class II, MPDI program, 22 students
November 2017
Week Coordinators: **Liesbeth Veenhoff, Michael Chang**
Objectives: Students acquire theoretical knowledge and practical experience in a number of techniques, are able to identify an appropriate technique and model system to solve a research question, and are able to design an appropriate experimental plan for a research question formulated after critical evaluation of recent articles.

"Molecular and Genetic Age Research at ERIBA"
6 weeks practical research course, 10 ECTS, 18 BSc biomedical students
June 2017
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 epi-genetics. Students should choose a first choice lab and a second choice lab.

"Specialization Track on the Biology of Ageing"
Master students in Biomedical Sciences (FWN), 20 students
Coordinator: **Ellen Nollen**
Objectives: Coordination and mentoring of students that want to specialize in aging research. The research track includes courses that have been developed and are coordinated by ERIBA PIs, which are i) Molecular Biology of Aging course and ii) Current themes in Health Ageing.

Learning Community Molecular Medicine.
January - September 2017, Bachelor program for medicine students.
Coordinator: **Gerald de Haan**
In 2014 a new bachelor curriculum for medicine students was implemented, referred to as G2020. Gerald de Haan lead a team that developed the -English taught- curriculum for ~95 students each year that enroll in the Molecular Medicine track.

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.

Media

November 11, 2017
Participation in the O&O Show "Food or Fiction"
Staff Members Involved: Cor Calkhoven

November 13-27, 2017
Talentenexpositie in de Stad, an initiative of City of Talent
Staff Members Involved: Cor Calkhoven

July 28, 2017
Contribution to a Volkskrant article under the title: "Je moet het maar durven: een ongetest middel injecteren"
www.volkskrant.nl/wetenschap/je-moet-het-maar-durven-een-ongetest-middel-injecteren~a4508424/
Staff Members Involved: Cor Calkhoven

Interview for City of Talent
www.cityoftalent.nl/blog/groningse-muis-leeft-langer-en-blijft-gezonder
Staff Members Involved: Cor Calkhoven

February 2, 2017
Interview for Digital Trends
www.digitaltrends.com/cool-tech/chemotherapy-side-effects-eliminated/
Staff Members Involved: Marco Demaria

February 8, 2017
Interview for the New Scientist
www.newscientist.com/article/mg23331122-300-drug-stops-nasty-chemotherapy-side-effects-in-mice-with-cancer/
Staff Members Involved: Marco Demaria

Events

October 14, 2017
Zpannend Zernike (open house at ERIBA)
Staff Members Involved: Anton Steen, Liesbeth Veenhoff, Judith Paridaen

February 2, 2017
Weekend van de Wetenschap
Staff Members Involved: Liesbeth Veenhoff


Erik Gietema

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
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Department of Biology
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The Pediatric Oncology Foundation Groningen (SKOG)

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