ERIBA

European Research Institute for the Biology of Ageing

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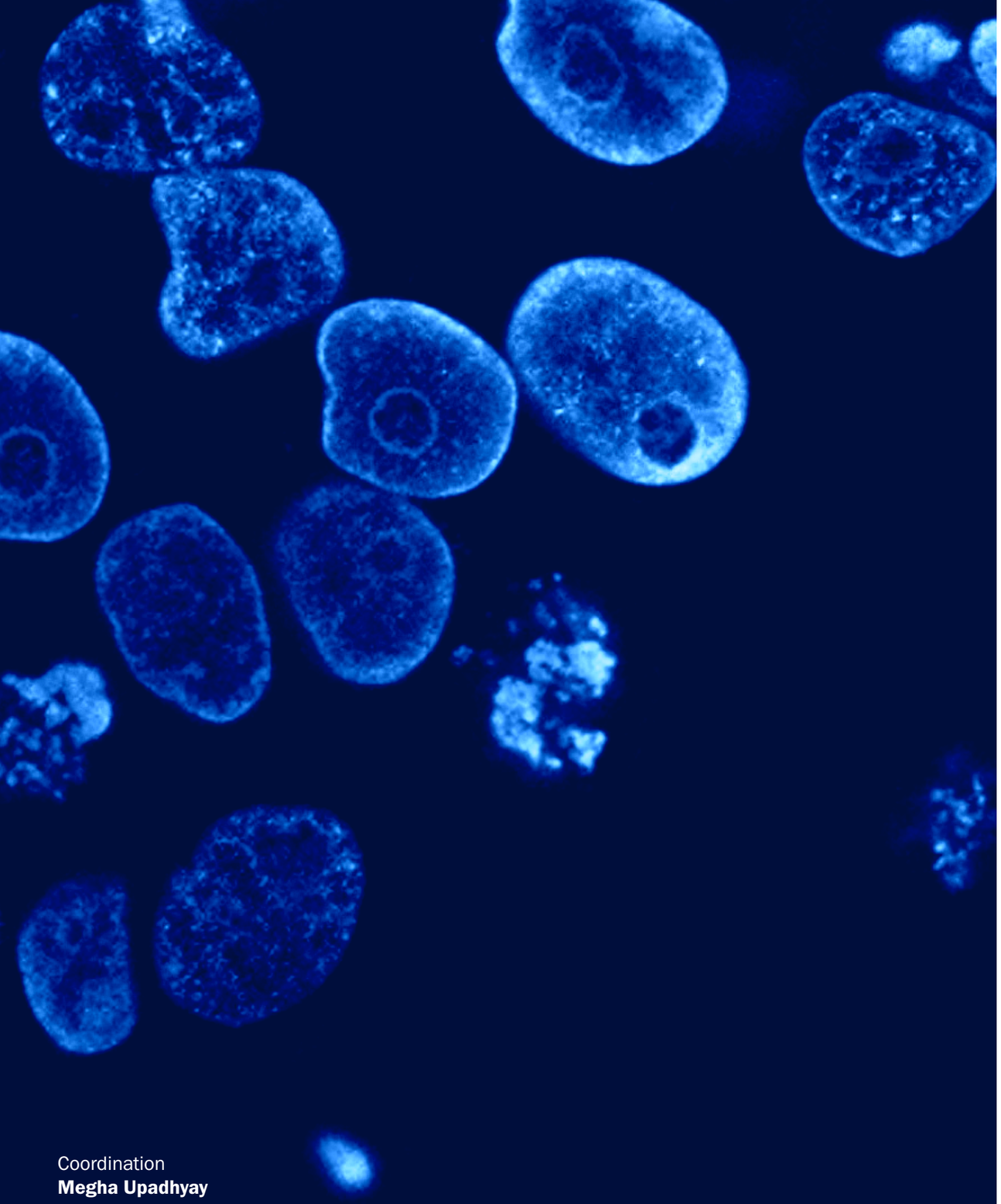
university of groningen



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FOREWORD BY THE DIRECTOR

We keep marching forward to elucidate the mechanisms that drive ageing, with a view to develop strategies to combat unhealthy ageing and age-related diseases.

It is with great pleasure to present to you the combined Annual Report 2022-2023 of the European Research Institute for the Biology of Ageing. We are proud to share with you our remarkable achievements, progress that has been accomplished in 2022 and 2023. These years have been outstanding with notable publications, funding, education and outreach activities, and appreciable collaborations.

I am delighted to share that we keep marching forward to elucidate the mechanisms that drive ageing, with a view to develop strategies to combat unhealthy ageing and age-related diseases. We published a record number of 57 papers in 2022 and 77 papers in 2023 showing our commitment to ageing research. These publications were the result of important scientific collaborations within ERIBA, with colleagues from the UMCG and with laboratories around the world . We cherish and thank all of our colleagues for this continuous collaboration. Looking forward to the future, we anticipate continuing and expanding our collaborations aimed at the advancement of ageing research.

In June 2023, the Dutch Society for Research on Ageing (DuSRA) was organized by our institute promoting synergy between fundamental and biomedical ageing research. In September 2023, ERIBA and the Leibniz Institute on Ageing-Fritz Lipmann Institute organized a joint meeting to foster collaborations, bringing together world-leading scientists to discuss the diverse research areas that are relevant for understanding the biology of ageing. We strongly encourage collaborations and these meetings/events help us achieve the objective of discovering critical ageing mechanisms and the development of new intervention strategies.

We are committed to talent development in the field of ageing research. In 2022 and 2023 excellent PhD students, undergraduates, and postdocs joined the institute and others left the institute to embark on future endeavours. It is great to see that numerous students have a keen interest in ageing research, and they carry out rotations in our institute.

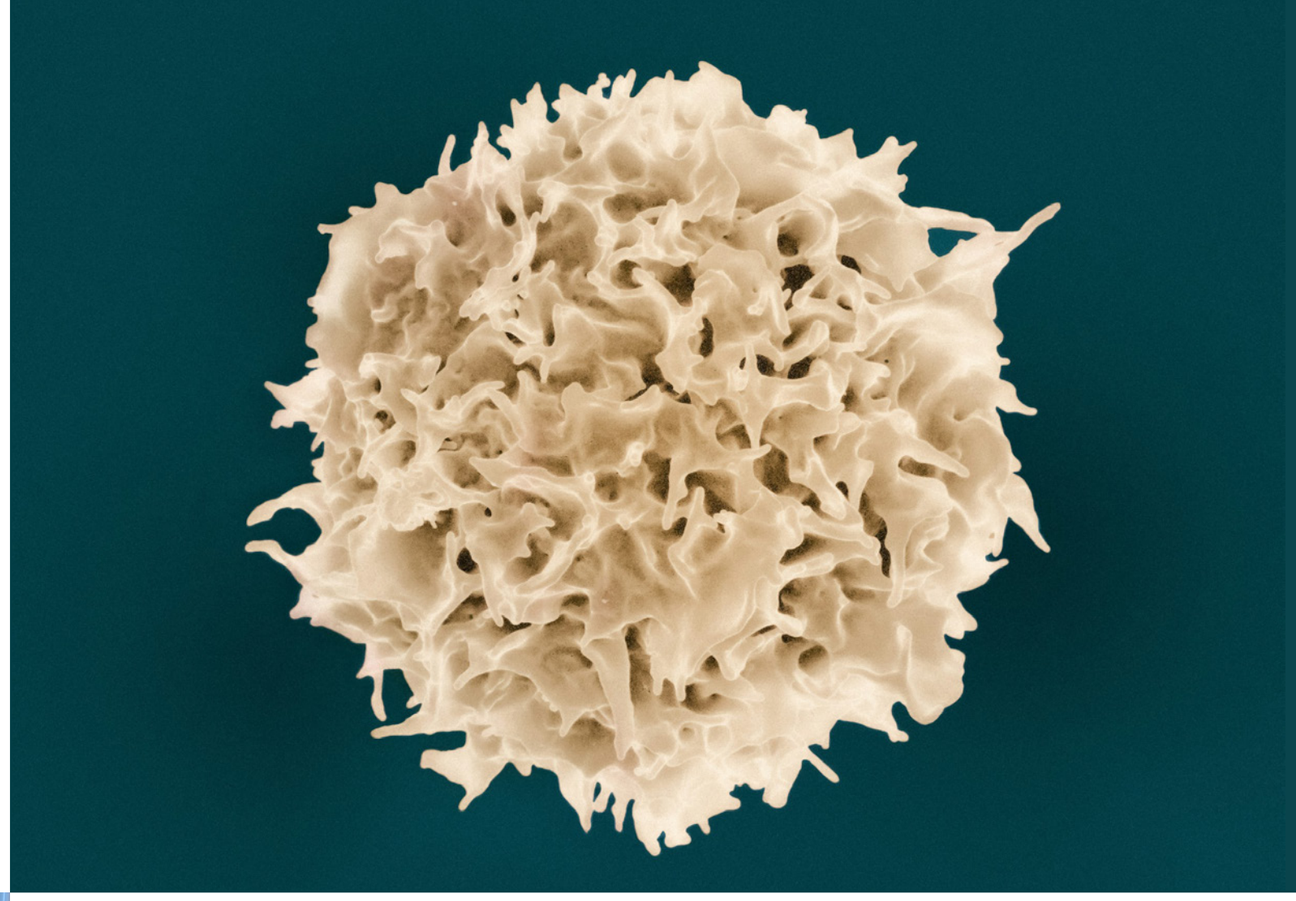
In 2022 and 2023, our scientists were once again successful in the acquisition of research funding, which includes prestigious and competitive national and global grants. Our scientists have also collaborated with biotech companies, leading to financed collaborative research projects in public-private partnerships. These collaborations have led to finding solutions for age-related diseases and such collaborations also show our commitment to prevention, delay, or reversal of the ageing process.

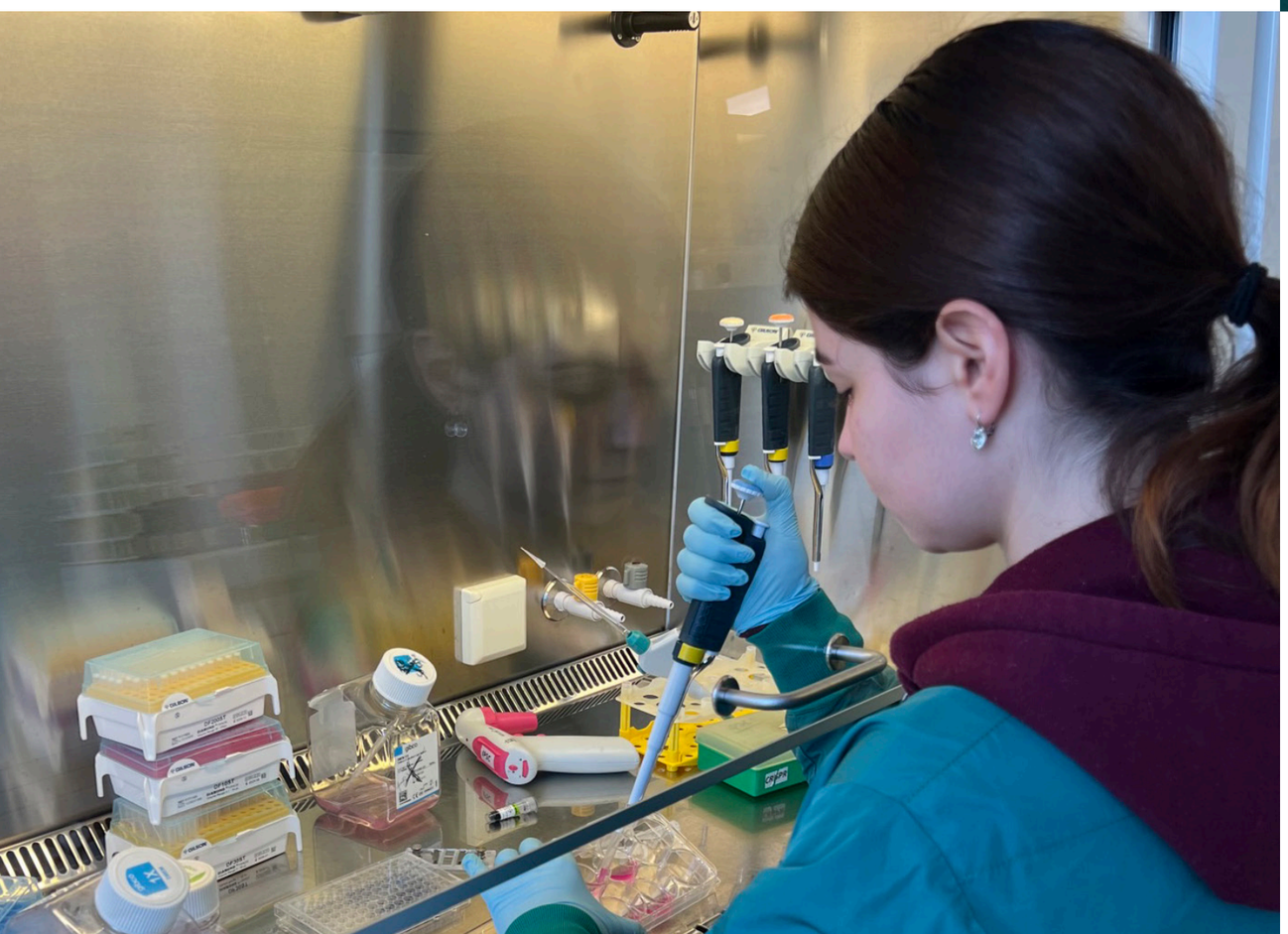
Knowledge sharing with society is of utmost importance, and I am delighted to share that our scientists were involved in many of the outreach activities. We hosted many outreach events for high school students and the public. Our presence on social media is also one of the many outreach efforts important for sharing our knowledge and findings with society.

Since 2023, ERIBA is part of a new cluster within the UMCG organization. This new cluster Biomedical Science and Technology is aimed at fostering collaborations, nurturing talents to showcase, achieve our ambition to become a global leading ageing institute for innovative research. I greatly appreciate the efforts and contributions of all the staff involved in paving the way for creating a global, highly reputed ageing institute with state of art facilities. I wish everybody all the best for future endeavours.

Folkert Kuipers

RESEARCH GROUPS AT ERIBA





ERIBA is an internationally recognized European research center on ageing.

The institute focuses on fundamental biology to understand the causes of ageing.

At ERIBA, studies are focused on the mechanisms that result in the loss of cells with age, and decline in function of old cells and tissues.

Eugene Berezikov

STEM CELL REGULATION AND MECHANISMS OF REGENERATION

INTRODUCTION

Resilience is the capacity of a complex system to recover from perturbations. In essence, ageing and age-related diseases are manifestations of the failing resilience of a living organism in the face of various intrinsic and extrinsic stresses. Some animal species evolved better resilience mechanisms than others, and investigating these mechanisms will broaden our understanding of the underlying fundamental biology and can eventually contribute to developing novel therapies in humans.

To this end, we study the model organism Macrostomum lignano – a flatworm that can regenerate its body, is long-lived and highly resistant to various stresses, including ionizing and UV radiation. To translate our findings in flatworms to other model organisms, we also utilize the nematode C. elegans and one of the shortest-living vertebrate models, the killifish Nothobranchius furzerii.

RESEARCH FOCUS

The flatworm Macrostomum lignano has an impressively advanced resilience, far beyond other animals (Fig. 1). Besides regeneration, it can also de-grow in the absence of food and survive long periods of starvation, and grow back when food becomes available again. It can live several years, and its mortality hazard does not increase with age. It sustains very high doses of ionizing radiation (120 Gy), as well as sterilization-level doses of ultraviolet C (100 mJ/cm2). We think that all these remarkable resilience properties of M. lignano are conferred primarily at the level of the stem cells (neoblasts), because as long as the neoblasts are functional, the damaged cells can be continuously replaced.

In order to start understanding the remarkable biology of this animal, in recent years we focused on developing a genetic toolbox for M. lignano. We identified stem cell and germline transcriptional signatures, sequenced, assembled and annotated the genome, and establishing a robust transgenesis method. Importantly, M. lignano is the only flatworm species in which transgenesis is available, and it allowed us to generate the first-ever stem-cell-specific M. lignano transgenic lines, which opens up tremendous research opportunities. Furthermore, we demonstrated that for its size the animal is remarkably long-lived (more than 2 years), and appears resilient to aging via active regulation of the stem cells. Next to M. lignano, we also use other Macrostomum species and an acoel Symsagittifera roscoffensis for comparative studies of stem cell regulation.

THE FUTURE

Regeneration is an efficient organismal resilience strategy to injury but understanding its mechanisms is still incomplete. Using the power of transgenesis in M. lignano, combined with single-cell sequencing and comparative genomics, we plan to characterize regulatory programs that drive cell fate specification during regeneration. Furthermore, we plan to investigate how M. lignano survives high doses of gamma- and UVC radiation and test whether resilience-associated Macrostomum genes can confer similar resilience in other animals.

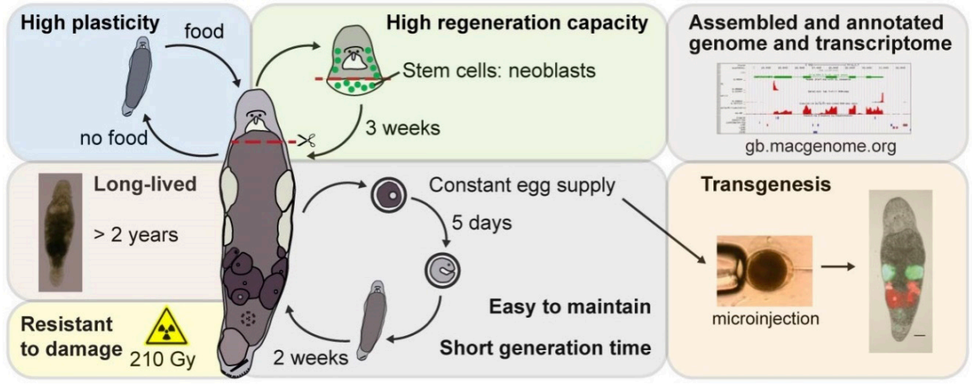


Figure 1. The flatworm Macrostomum lignano is a versatile model organism to study stem cells, regeneration, ageing and resilience mechanisms. Adapted from Wudarski et al., EvoDevo 11:5 (2020).

SELECTED PUBLICATION

Genome assembly of the acoel flatworm Symsagittifera roscoffensis, a model for research on body plan evolution and photosymbiosis

Pedro Martinez, Kirill Ustyantsev, Mikhail Biryukov, Stijn Mouton, Liza Glasenburg, Simon G Sprecher, Xavier Bailly, Eugene Berezikov

G3 (Bethesda). 2023 Feb 9;13(2):jkac336. doi: 10.1093/g3journal/jkac336.

Symsagittifera roscoffensis is a well-known member of the order Acoela that lives in symbiosis with the algae Tetraselmis convolutae during its adult stage. Its natural habitat is the eastern coast of the Atlantic, where at specific locations thousands of individuals can be found, mostly, lying in large pools on the surface of sand at low tide. As a member of the Acoela it has been thought as a proxy for ancestral bilaterian animals; however, its phylogenetic position remains still debated. In order to understand the basic structural characteristics of the acoel genome, we sequenced and assembled the genome of aposymbiotic species S. roscoffensis. The size of this genome was measured to be in the range of 910-940 Mb. Sequencing of the genome was performed using PacBio Hi-Fi technology. Hi-C and RNA-seq data were also generated to scaffold and annotate it. The resulting assembly is 1.1 Gb large (covering 118% of the estimated genome size) and highly continuous, with N50 scaffold size of 1.04 Mb. The repetitive fraction of the genome is 61%, of which 85% (half of the genome) are LTR retrotransposons. Genome-guided transcriptome assembly identified 34,493 genes, of which 29,351 are protein coding (BUSCO score 97.6%), and 30.2% of genes are spliced leader trans-spliced. The completeness of this genome suggests that it can be used extensively to characterize gene families and conduct accurate phylogenomic reconstructions.

GROUP MEMBERS

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Cor Calkhoven

GENE REGULATION IN AGEING AND AGE-RELATED DISEASES

INTRODUCTION

Our research aim is to identify and understand the role of regulatory networks that control the function of C/EBPα and C/EBPβ transcription factors in ageing and age-related diseases. We showed that mRNA-translational regulation of C/EBPβ expression through the mTORC1 nutrient and energy signaling pathway are linked to ageing and health- and lifespan determination. Others showed that deficiency of DNA-demethylation factors that regulate access of C/EBPβ to its genome binding sites result in premature ageing. In addition, the NAD+-SIRT1 pathway controls the function in mitochondrial biogenesis and respiration through regulation of C/EBPα protein-deacetylation. Apart from its physiologic metabolic functions, we study the oncogenic functions of C/EBPβ in promoting cancer metabolism, cell migration and immune evasion, particular in breast cancer. In another line of research, we study the pro-tumorigenic role of TSC-mTORC1 regulation in small cell lung cancer and its potential value as a therapeutic target.

RESEARCH FOCUS

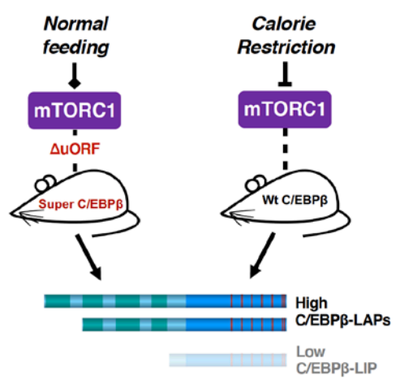
CEBPA- and CEBPB-mRNAs are translated into complete and active transcription factors, called C/EBPβ-LAP and C/EBPα-p42 as well as into shorter inhibitory factors, called C/EBPβ-LIP and C/EBPα-p30. A single uORF in the mRNAs acts as a cis-regulatory element required for translation into LIP and p30 and confers sensitivity to specific translational regulation pathways, in particular to mTORC1 nutrient signaling. We have shown that hindering mTORC1 from regulating LIP by removal of the uORF results in a wide range of delays in age-related conditions in mice, akin those observed by calorie restriction or other mTOIRC1 inhibitory measures (Figure). This Cebpb$^{\Delta uORF}$ mutation is characterized by C/EBPβ super-function since only the transactivating LAP is expressed, unrestrained by expression of the inhibitory LIP. We know that the C/EBPα-p30 expression is similarly regulated and that removal of the uORF results in C/EBPα super-function in cell culture. Physiological relevance of p30 regulation awaits examination of Cebpa$^{\Delta uORF}$ mice that just have been generated.

Another prominent regulation of C/EBPα function is through lysine-acetylation. The acetylation status of C/EBPα is controlled through deacetylation by SIRT1 in response to changes in NAD$^+$ homeostasis. Hypoacetylated C/EBPα stimulates the transcription of mitochondrial genes and results in increased mitochondrial function, identifying C/EBPα as a key mediator of SIRT1-controlled adaption of energy homeostasis. Preliminary data of studies deciphering the molecular mechanisms behind the differential gene regulation by hypo- versus hyperacetylation C/EBPα suggest the involvement of cofactor switching.

In another line of research, we discovered that oncogenic MYC restrains mTORC1 signaling in Burkitt's lymphoma by safeguarding the expression of the tuberous sclerosis complex (TSC). Interference with MYC-TSC1-mTORC1 regulation results in enhanced mitochondrial respiration, accumulation of toxic reactive oxygen species and cell death. Our current studies show that TSC expression is also high in small cell lung cancer and we currently investigate its tumor promoting role and involved regulatory and pathological mechanisms.

THE FUTURE

We will investigate the role of mTORC1- and SIRT1-C/EBPα regulation in health and lifespan determination using genetic engineered mouse and killifish models. The role C/EBPβ in breast cancer development and cancer immune evasion will be studied. We have identified RNA-methylation as a new regulatory stage of C/EBPs as well as other regulatory factors in metabolism and cancer that will require further investigations. As part of both the C/EBP and TSC projects we aim to develop drug screening strategies in order to develop new therapies for metabolic disorders and cancer.



Metabolic trait	C/EBPβ −ΔuORF	Calorie restricted
Body weight	↓	↓
Fat content	↓	↓
Steatosis	↓	↓
Adiponectin	↑	↑
Glucose	↓	↓
Insulin	↓	↓
Glucose tol.	↑	↑
Ins. sensitivity	↑	↑
GH/IGF-1	↓	↓

Ageing phenotypes	C/EBPβ −ΔuORF	Calorie restricted
Rotarod	↑	↑
Beam walking	↑	↑
Wire hang	↑	↑
naïve/memory T-cells	↑	↑
Better maintained during ageing (4 vs. 20 months)		
Cancer	↓	↓

Figure 1: The table shows a compilation of phenotypes induced by the Cebpb$^{\Delta uORF}$ mutation resulting in C/EBPβ super-function through loss of LIP expression. Simmilar metabolic phenotypes and delay in age-related conditions can be achieved by calorie restriction.

SELECTED PUBLICATION

Ackermann, T., Zuidhof, H.R., Müller, C., Kortman, G., Rutten, M.G.S., Broekhuis, M.J.C., Zaini, M.A., Hartleben, G. and **Calkhoven, C.F.** (2023) C/EBPβ-LIP mediated activation of the malate-aspartate shuttle sensitizes cells to glycolysis inhibition. Mol Metab. DOI: 10.1016/j.molmet.2023.101726

Objective Cancer cells use glycolysis for generation of metabolic intermediates and ATP needed for cell growth and proliferation. The transcription factor C/EBPβ-LIP stimulates glycolysis and mitochondrial respiration in cancer cells. We initially observed that high expression of C/EBPβ-LIP makes cells vulnerable to treatment with the glycolysis inhibitor 2-deoxyglucose. The aim of the study was to uncover the involved mechanisms of C/EBPβ-LIP induced sensitivity to glycolysis inhibition.

Methods We used genetically engineered cell lines to examine the effect of C/EBPβ-LIP and -LAP protein isoforms on glycolysis and NADH/NAD+ metabolism in mouse embryonic fibroblasts (MEFs), and triple negative breast cancer (TNBC) cells that endogenously express high levels of C/EBPβ-LIP. Analyses included assays of cell proliferation, cell survival and metabolic flux (OCR and ECAR by Seahorse XF96). Small molecule inhibitors were used to identify underlying metabolic pathways that mediate sensitivity to glycolysis inhibition induced by C/EBPβ-LIP.

Results The transcription factor C/EBPβ-LIP stimulates both glycolysis and the malate-aspartate shuttle (MAS) and increases the sensitivity to glycolysis inhibition (2-deoxyglucose) in fibroblasts and breast cancer cells. Inhibition of glycolysis with ongoing C/EBPβ-LIP-induced MAS activity results in NADH depletion and apoptosis that can be rescued by inhibiting either the MAS or other NAD$^+$-regenerating processes.

Conclusion This study indicates that a low NADH/NAD$^+$ ratio is an essential mediator of 2-deoxyglucose toxicity in cells with high cytoplasmic NAD$^+$-regeneration capacity and that simultaneous inhibition of glycolysis and lowering of the NADH/NAD$^+$ ratio may be considered to treat cancer.

GROUP MEMBERS

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Gertrud Kortman Technician

Michael Chang

TELOMERES AND GENOME INTEGRITY

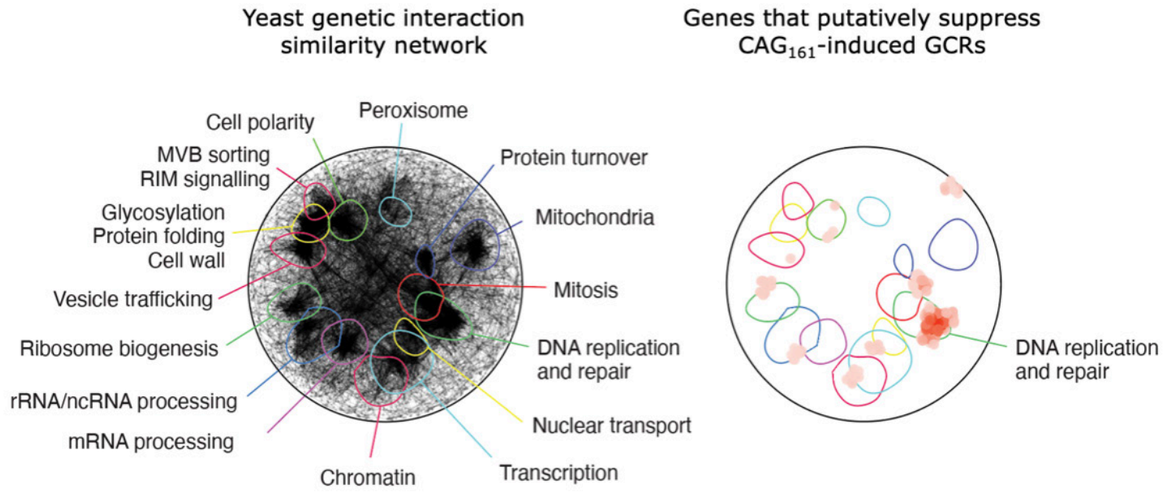

Figure legend: A screen for suppressors of (CAG)161-induced chromosomal breakage identified many genes involved in DNA replication and repair. The left panel depicts the yeast genetic interaction similarity network annotated with gene ontology biological process terms to identify major functional domains (Costanzo et al., 2016; doi: 10.1126/science.aaf1420). Genes are connected by a line if they share a similar genetic interaction profile, and genes sharing more similar genetic interaction profiles are positioned closer together. On the right, regions of the network enriched for genes identified in the (CAG)161 screen were mapped using the SAFE (spatial analysis of functional enrichment) method (Baryshnikova, 2016; doi: 10.1016/j.cels.2016.04.014).

INTRODUCTION

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

RESEARCH FOCUS

Research in our lab is currently focussed on understanding:

How structures called telomeres protect the ends of our chromosomes

Telomeres consist of short tandem repetitive sequences bound by specialized proteins. They help distinguish natural chromosome ends from DNA breaks in need of repair. Dysfunctional telomeres result in DNA damage checkpoint activation and cell cycle arrest. Telomeres progressively shorten due to incomplete DNA replication and nucleolytic degradation. When telomeres are critically shortened, cells can no longer divide, reaching a state known as replicative senescence. Shortening is counteracted by telomerase, the specialized reverse transcriptase that elongates telomeres. However, most human somatic cells do not express sufficient telomerase to prevent telomere shortening, which has been proposed as one reason why human individuals age. Replicative senescence is thought to function as a barrier to tumorigenesis since cancer cells need to maintain telomeres to continue proliferating.

How cells deal with DNA sequences that are particularly challenging to replicate or repair

Short tandem DNA repeat sequences account for approximately 3% of the human genome. These sequences are often difficult to replicate, are prone to expansion and contraction, and can cause chromosomal rearrangements. Expansion of 13 different short tandem repeat sequences is linked to approximately 50 diseases, including Huntington's disease, Friedreich's ataxia, and fragile X syndrome, while chromosomal rearrangements are a source of genetic diseases and cancer. Misregulation of telomeric repeats, a well-studied example of a short tandem repeat sequence, is a hallmark of both cancer and ageing.

We examine these processes at a molecular level using the budding yeast Saccharomyces cerevisiae, which is an ideal model organism given the highly conserved nature of these processes and the experimental advantages of the yeast system. We aim to identify relevant genes, and to determine their function and relationship with one another.

THE FUTURE

Our lab will continue to study how cells protect their genome from the accumulation of mutations, chromosomal rearrangements, and telomere dysfunction. In particular, we are focussed on understanding how repetitive DNA sequences, which pose unique obstacles for the DNA replication machinery, are dealt with by genome maintenance mechanisms.

SELECTED PUBLICATION

Yao, Y., Fekete-Szücs, E., Rosas Bringas, F.R., and **Chang, M.** (2023) Deletion of MEC1 suppresses the replicative senescence of the cdc13-2 mutant in *Saccharomyces cerevisiae*. ***G3: Genes, Genomes, Genetics***, 13(5): jkad065.

In *Saccharomyces cerevisiae*, telomerase recruitment to telomeres depends on a direct interaction between Cdc13, a protein that binds single-stranded telomeric DNA, and the Est1 subunit of telomerase. The cdc13-2 allele disrupts telomerase association with telomeres, resulting in progressive telomere shortening and replicative senescence. The Mec1/ATR kinase is both a positive and a negative regulator of telomerase activity and is required for the cell cycle arrest in telomerase-deficient senescent cells. In this study, we find that the deletion of MEC1 suppresses the replicative senescence of cdc13-2. This suppression is dependent on telomerase, indicating that Mec1 antagonizes telomerase-mediated telomere extension in cdc13-2 cells to promote senescence.

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Marco Demaria

CELLULAR SENESCENCE AND AGE-RELATED PATHOLOGIES

INTRODUCTION

Our research focuses on the mechanisms that regulate induction and development of cellular senescence, and the heterogeneous physiological and pathological functions of senescent cells. Senescence-associated growth arrest represents a well-established tumor suppressive mechanism but can cause inability to maintain important cell pools with age. Remarkably, most senescent cells secrete a collection of various cytokines, growth factors, matrix metalloproteases, lipids and nucleotides – a phenotype known as SASP (senescence-associated secretory phenotype). The SASP plays an essential role in tissue remodeling and repair during embryogenesis and adulthood, and guarantees effective clearance of senescent cells. However, increasing evidence indicates that senescent cells accumulate in tissues of older organisms where the SASP contributes to chronic low-level inflammation and aberrant tissue growth and remodeling. The identification of deleterious pro-disease senescent cells prompted the development of senolytic drugs able to induce selective death of senescent cells.

RESEARCH FOCUS

Our laboratory has pioneered the concept of senescence heterogeneity by performing a comprehensive transcriptomic study to different senescence subsets. These data together with data from other laboratories have demonstrated that several intrinsic and extrinsic factors contribute to regulate induction and development of senescence-associated phenotypes. Importantly, we have defined that different subsets of senescent cells – each characterized by particular combinations of senescence-associated phenotypes – can co-exist in vivo, but specific molecular characteristics of these different populations remain largely unknown. Identification of senescence subset-specific molecular marks can help to unequivocally characterize physiological and pathological functions of cellular senescence. To reach this goal, we are using senescence-reporter mice to study aging and diseases associated to senescent cells. In addition, we are developing mice lacking genes that we have identified as part of the core signature of senescence.

To dissect between beneficial and detrimental senescence programs we are using various models. For beneficial senescence, we use models of skin, muscle and kidney injury. For detrimental senescence, we are using a number of disease models including cancer, osteoarthritis and chronic kidney disease. We are also planning to exploit the knowledge acquired during this analyses to modulate senescence-associated phenotypes and/or promote or eliminate senescent cells.

Modulation of senescence in vivo can be achieved both via pharmacological or lifestyle interventions. We have recently demonstrated that combining repurposed anti-apoptotic inhibitors is sufficient to remove senescent melanocytes and eliminate nevi in the mouse skin (Figure 1; Kohli J et al, Nat Comms, 2022).

We have also shown that diets with low-protein and low-fat intake and endurance exercise prevents the accumulation of cellular senescence in mice and humans (Nehme et al, FEBS J, 2022; Demaria M et al, npj aging, 2023).

Our laboratory is actively characterizing how new small molecules and exposure to environmental conditions and lifestyle interventions can influence the accumulation of senescent cells with aging.

THE FUTURE

In the future we aim to expand our understanding on senescence heterogeneity by analyzing and phenotyping senescence subsets associated to specific physiological and pathological conditions. Our goal is to contribute to the understanding of the multifaceted role of senescence and to the development of potent anti-aging and disease interventions. To reach this goal, we have established collaborations with several clinical departments and with different biotech and pharma companies.

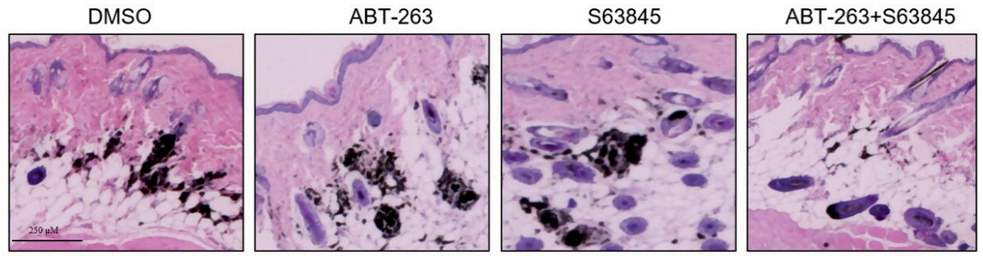

Figure 1. Nevi or pigmented lesions (in black) were induced on the dorsal skin of mice. The indicated anti-apoptotic inhibitors (or DMSO as control) were topically applied. The combination of ABT-263 (BCL-2 inhibitor) and S63845 (MCL-1 inhibitor) show a dramatic reduction in the size of the pigmented lesion.

SELECTED PUBLICATION

Targeting anti-apoptotic pathways eliminates senescent melanocytes and leads to nevi regression

Jaskaren Kohli 1, Chen Ge 1, Eleni Fitsiou 1, Miriam Doepner 2, Simone M Brandenburg 1, William J Faller 3, Todd W Ridky 2, **Marco Demaria**

DOI: 10.1038/s41467-022-35657-9

Human melanocytic nevi (moles) result from a brief period of clonal expansion of melanocytes. As a cellular defensive mechanism against oncogene-induced hyperplasia, nevus-resident melanocytes enter a senescent state of stable cell cycle arrest. Senescent melanocytes can persist for months in mice and years in humans with a risk to escape the senescent state and progress to melanoma. The mechanisms providing prolonged survival of senescent melanocytes remain poorly understood. Here, we show that senescent melanocytes in culture and in nevi express high level of the anti-apoptotic BCL-2 family member BCL-W but remain insensitive to the pan-BCL-2 inhibitor ABT-263. We demonstrate that resistance to ABT-263 is driven by mTOR-mediated enhanced translation of another anti-apoptotic member, MCL-1. Strikingly, the combination of ABT-263 and MCL-1 inhibitors results in synthetic lethality to senescent melanocytes, and its topical application sufficient to eliminate nevi in male mice. These data highlight the important role of redundant anti-apoptotic mechanisms for the survival advantage of senescent melanocytes, and the proof-of-concept for a non-invasive combination therapy for nevi removal.

GROUP MEMBERS

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GENOMIC INSTABILITY IN DEVELOPMENT AND DISEASE

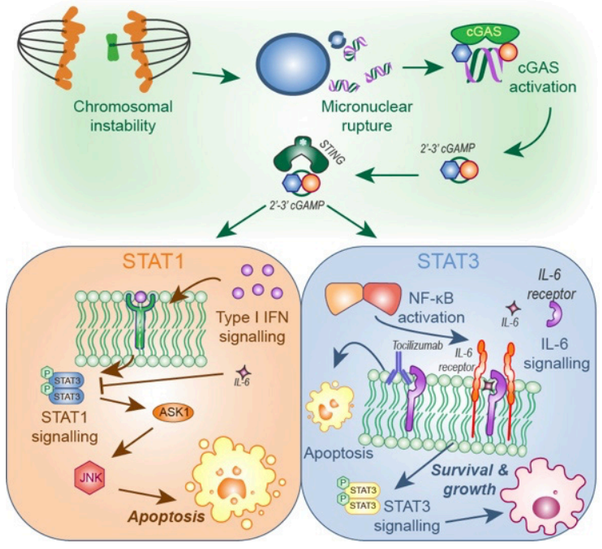
INTRODUCTION

Chromosomal instability (CIN) is a hallmark feature of cancer. CIN leads to cells with an abnormal DNA content, a state known as aneuploidy affecting >80% of all cancers. Paradoxically, in untransformed cells, CIN and aneuploidy decrease cellular fitness and lead to activation of stress pathways. This suggests that cancer cells have found ways to cope with the downsides of CIN. A better understanding of these coping strategies can lead to new therapies that target these mechanisms, and thus selectively kill the aneuploid cancer cells with fewer side effects on healthy cells. We study the how cells deal with chromosomal instability and aneuploidy, in vitro as well as in vivo. For this we 1) develop and exploit models and technology to faithfully measure chromosomal instability and aneuploidy in cultured cells as well as in living mice, 2) we develop mouse and advanced cell models to study CIN, which we 3) use to better understand the mechanisms that trigger the responses to CIN and 4) we exploit these mechanistic findings to design therapies that selectively kill cells with a CIN phenotype.

RESEARCH FOCUS

Ongoing CIN leads to cells with variable karyotypes and thus to intratumour karyotype heterogeneity. CIN is therefore a strong driver of cancer cell evolution and associated with poor prognosis. Together with the research sequencing facility, we heavily invested in single cell DNA sequencing as a tool to quantify karyotype heterogeneity. We for instance used this tool to study how newly developed tools that can induce missegregation of a single chromosome perform (refs 1, 2). Furthermore, to better understand how chromosome missegregation affects the fitness of individual cells, we combine scWGS and scRNA-seq to better understand how individual karyotypes influence cellular fitness. For this, we take advantage of our earlier-published mouse models of CIN-induced T-ALL, from which we analyze primary tumor samples as well as T-ALL-derived cell lines, which is revealing that tumors with an ongoing CIN phenotype and semi-clonal karyotypes contain multiple smaller clones with unique karyotypes. We are currently investigating the biology of these smaller clones to better understand how chromosome missegregation drives cancer cell evolution, but also how CIN leads to cell populations that are less fit that ultimately will be selected against.

We recently found that CIN will trigger an inflammatory response in premalignant as well as cancer cells. Our work is indicating that this inflammatory response activates the immune system and thus leads to immune clearance of premalignant aneuploid cells. We find that cancer cells circumvent this inflammatory response by alleviating one of the main inflammatory routes in the cell: STAT1 signaling. This inflammatory response, triggered by CIN, critically relies on IL6 activity upstream of Stat1 and Stat3. In 2022, we showed that blocking IL6 signaling, e.g. by means of the clinically approved IL6R inhibitor tocilizumab is toxic to CIN tumor cells in vitro and in vivo, but well-tolerated by chromosomal stable cancers, revealing an unexpected Achilles heel of aneuploid cancers, which we are currently validating in models for T-ALL (funded by a Lymph&Co grant) and breast cancer (funded by a Vici grant). In a separate research line, in collaboration with the Functional Genomics Center, using ALS patient-derived iPSCs, we discovered that mutant-FUS-driven ALS patients might benefit from IFN treatment as IFN signaling appears to protect FUS-mutant iPSC-derived motor neuron from oxidative stress (selected reference).



CIN leads to a STAT1 pro-death and STAT3 pro-survival inflammatory response that can be selectively targeted to kill cells with CIN.

THE FUTURE

Now that we identified that lack of immunosurveillance is an essential feature of tumors displaying a CIN phenotype, we next want to understand which immune cells clear aneuploid cells and which interactions between immune cells and cancer cells trigger clearance. Further, we want to map the molecular mechanisms that cancers exploit to inactivate immune signaling and translate this knowledge into therapeutic interventions that selectively target aneuploid cells. For this, we are developing state-of-the art cellular reporters to read out inflammation and techniques such as CUT&Tag to map the transitional response to CIN. In addition to mapping how immune cells clear aneuploid cells, we will also further investigate the molecular mechanisms that trigger the initial inflammation response, including CRISPR genome-wide screens.

Furthermore, we want to better understand how karyotype dynamics drive tumor evolution. For this, we will investigate how chromosome copy number changes change cellular fitness in cell models, but also in vivo, including intravital imaging models to visualize aneuploidy in vivo in zebrafish and, ultimately, in mice. For this, we will develop fitness reporters as well as new zebrafish and mouse models in which we can determine cellular fitness in cultured cells including genome-wide screens as well as in vivo.

SELECTED PUBLICATION

Assoni AF, Guerrero EN, Wardenaar R, Oliveira D, Bakker PL, Alves LM, Carvalho VM, Okamoto OK, Zatz M, **Foijer F#**. IFN protects motor neurons from oxidative stress via enhanced global protein synthesis in FUS-associated amyotrophic lateral sclerosis. Brain Pathol. 2023 Aug 15:e13206. doi: 10.1111/bpa.13206.

Amyotrophic lateral sclerosis type 6 (ALS6) is a familial subtype of ALS linked to Fused in Sarcoma (FUS) gene mutation. FUS mutations lead to decreased global protein synthesis, but the mechanism that drives this has not been established. Here, we used ALS6 patient-derived induced pluripotent stem cells (hIPSCs) to study the effect of the ALS6 FUSR521H mutation on the translation machinery in motor neurons (MNs). We find, in agreement with findings of others, that protein synthesis is decreased in FUSR521H MNs. Furthermore, FUSR521H MNs are more sensitive to oxidative stress and display reduced expression of TGFβ- and mTORC gene pathways when stressed. Finally, we show that IFN treatment reduces apoptosis of FUSR521H MNs exposed to oxidative stress and partially restores the translation rates in FUSR521H MNs. Overall, these findings suggest that a functional IFN response is important for FUS-mediated protein synthesis, possibly by FUS nuclear translocation in ALS6.

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Tovini L., Johnson S.C., Andersen A.M., Spierings D.C.J., Wardenaar R., **Foijer F.**, McClelland S.E#. Inducing Specific Chromosome Mis-Segregation in Human Cells. EMBO J. 2023 Apr 17:e111587. doi: 10.15252/embj.2022111587

Truong M.Y., Cané-Gasull P., de Vries S.G., Nijenhuis W., Wardenaar R., Kapitein L.C., **Foijer F.**, Lens S.M.A#. A motor-based approach to induce chromosome-specific mis-segregations in human cells. EMBO J. 2023 Apr 11:e111559. doi: 10.15252/embj.2022111559

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Marsudi Siburian PhD student
Maria Suarez Postdoc
Ruifang Tian PhD student
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Anouk van den Brink PhD student
Soraya Wobben PhD student
Siqi Zheng PhD student

Victor Guryev

GENOME STRUCTURE AGEING

INTRODUCTION

Even though the completion of the human genome project was announced over 20 years ago, our knowledge of genome variants and their effects on the onset of ageing-related diseases is still far from being complete. Under-investigated large and complex alterations in our genomes affect more DNA bases than single-nucleotide changes. Some of these structural genome changes can be predicted using a routine analysis procedure of DNA data, others, like large inversions or non-reference insertions, deserve further investigation.

Our research aims to identify a wide spectrum of DNA alterations, fine-map them to corresponding genomic locations, and characterize their effects on molecular function. Our group combines analysis of genome, transcriptome, and proteome profiling (functional genomics and proteogenomics approaches) to distinguish deleterious genomic variants from benign ones. These results should contribute to a better understanding of the content and function of variable segments in our genomes.

RESEARCH FOCUS

Our research is focused on several approaches for investigating ageing-related molecular changes:

A. Investigation of genome alterations potentially associated with ageing-related diseases (Fig 1A). We are studying the distribution and role of large variants in our genomes. My team applies expertise developed in the Dutch genome project to characterize SVs in patients suffering from early-onset severe COPD, cancer, and other diseases.

B. Transcriptome regulation in ageing and onset of diseases (Fig 1B). Previous studies already identified several trends (e.g. more retained introns) in transcriptome processing that happen as we get older. Our group analyses transcriptomes of several patient cohorts to identify sources of these changes and their potential roles in disease etiology.

C. Combining differential expression and differential variability analysis (Fig 1C). Since many human diseases are very heterogeneous in their molecular and clinical manifestations, molecular subtyping and analysis of differential variability provide orthogonal approaches to classical disease association methods. We successfully employed methods for quantifying biological variability to get insight into cellular processes affected by ageing, lung diseases, sepsis, and COVID-19.

D. Multi-level data integration for personalized diagnostics and treatment (Fig 1D). Combining DNA variation data with other omics layers, such as gene expression, proteomics, metabolomics, and phenotypic data, is key for the discovery of function for DNA polymorphisms. Previously, we used a rat model of hypertension to demonstrate that such analysis of DNA, RNA, and proteins, where information ‘flows’ across omics-layers, is an efficient way to study disease (PMID:24290761). This observation supports the validity of our approach and suggests that it can be useful for studying relations between structural genome variants and molecular phenotypes that manifest themselves at RNA and protein levels and potentially play roles in human diseases.

THE FUTURE

In the future, we aim to improve the prediction of functional consequences for large genome alterations in relation to human diseases. We plan to identify new transcriptional units and novel isoforms for known genes and link them to genome variation and dysregulated splicing factors (age- and disease-specific). Our short-term goal is to employ pathway and biochemical complex-centered analysis of gene expression variability. This will allow us to identify disruptions in particular gene ensembles on disease and better understand its underlying mechanism. Finally, we will continue to develop our computational framework for personalized multi-omics data integration and will utilize it for the analysis of omics data from other ageing-related diseases.

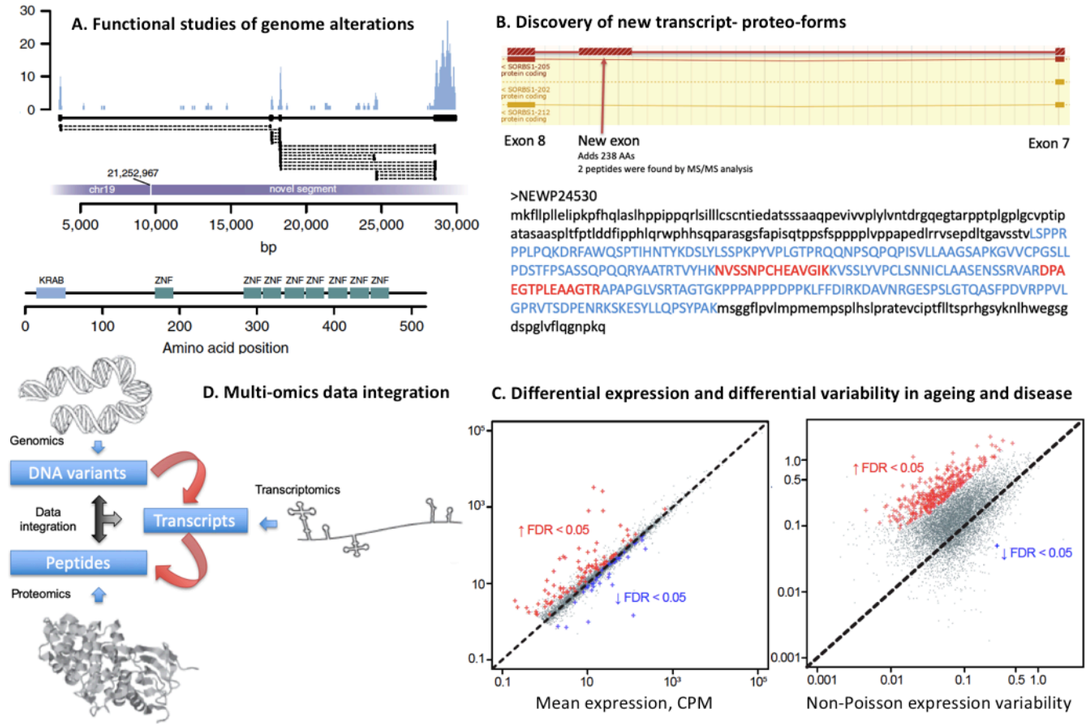

Figure 1. Major research directions. (A). Investigation and functional characterization of large genome alterations and their role in the onset of age-related diseases. An example of a long non-reference insert on chr19, that encodes for a new zinc finger gene. Transcript coverage by RNA-seq reads (top), reads supporting splicing events (middle), and domain structure of resulting protein product (bottom) are displayed. (B) Transcriptome analysis identifies new disease-associated protein-coding exons. An example of an exon in SORBS1 gene that is differentially present in transcripts of COPD patients. The exon adds 238 amino acids to the protein product and was confirmed by 2 corresponding peptides (in red) with LC-MS/MS data. (C) Differential expression and differential variability analysis show age-specific changes in gene expression. Left panel: more genes show upregulation of expression level in old individuals (y-axis) compared to young (x-axis). Right panel: many more genes show an increase in inter-individual variability in old individuals (y-axis) than in young individuals (x-axis). (D) Our multi-omics data integration approach. A common analysis strategy is to perform separate analyses for each omics level using public reference (black arrows). In our studies, we perform sequential integration where each omics layer informs the analysis of the next levels by providing data on DNA variants (genomics), splice variants, and new transcript units (transcriptome) for better interpretation of ageing- and disease-related molecular changes.

SELECTED PUBLICATION

Naslavsky MS, et al.. 2022. Whole-genome sequencing of 1,171 elderly admixed individuals from São Paulo, Brazil. Nat Commun. 13:1004. doi: 10.1038/s41467-022-28648-3.

Together with our PhD students (S. Zverinova and T. Karp), we established an international collaboration to investigate the role of non-reference sequences in the genomes of wellderly (elderly and healthy) Brazilians. We employed data from fully sequenced genomes of 1171 individuals from Sao Paulo to identify and characterize these missing segments. We identified a total of 67,4 million bases of non-redundant non-reference sequences missing from current human reference. We showed that the inclusion of NR segments improves both the mapping and analysis of sequencing data. We identified many population-specific sequences (a total of 9.3 million bases) and explored potentially coding parts of the new DNA. This manuscript is very broad and describes different aspects of Brazilian genomes (from inter-individual variability, and population structure to utility for GWAS mapping), and our important contribution was to locate, describe, and evaluate regions that would escape their interpretation because of existing bias of reference datasets that are lacking genomic data from South-America.

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MOLECULAR NEUROBIOLOGY OF AGEING

INTRODUCTION

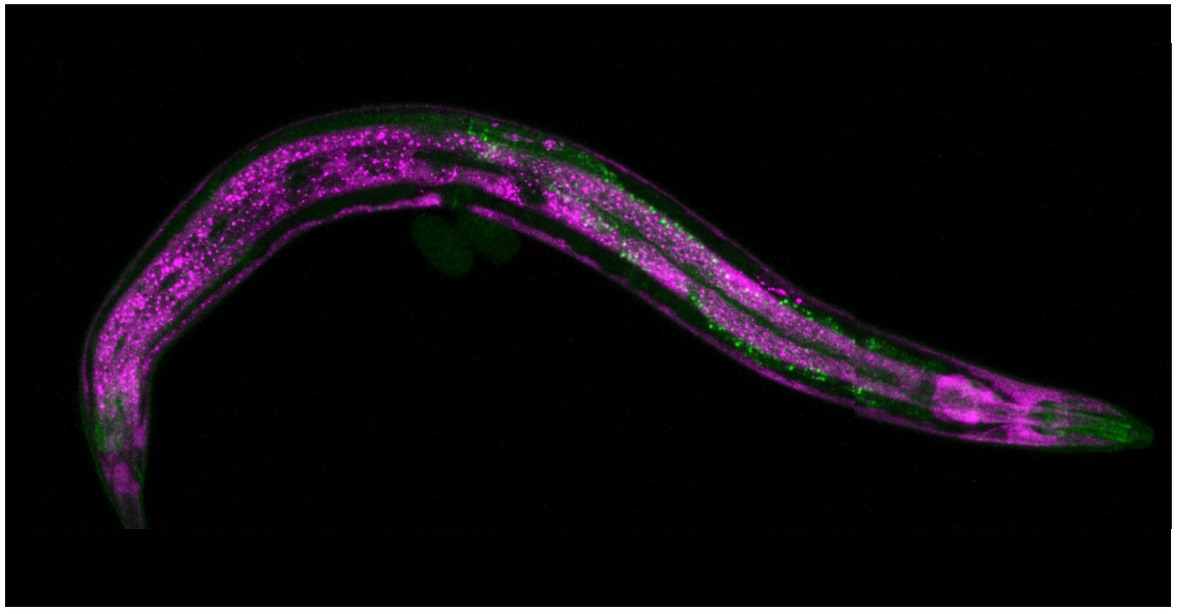
Maintenance of protein homeostasis is essential for cellular health but during aging cellular maintenance mechanisms become less effective. Due to this loss of protein homeostasis, aggregation-prone proteins accumulate, which are toxic to cells and can cause disease. The biological mechanisms that drive such age-related protein toxicity are still incompletely understood. Our aim is to uncover these mechanisms and identify targets for biomedical interventions that prevent or delay age-related protein toxicity in aging and age-related diseases.

RESEARCH FOCUS

Our research focusses on aggregation-prone proteins that are characteristic of proteinopathies like Parkinson, Alzheimer's and ALS, which include alpha-synuclein, amyloid-beta, and TDP-43, and the mechanisms that drive their toxicity. Using genetic and phenotypic screens in C. elegans models, we have identified several evolutionary conserved mechanisms that, when inhibited, suppress the toxicity of such disease proteins. These include cellular factors like MOAG-4/SERF that drives toxicity through direct, charge-driven, interactions with aggregation-prone proteins. In addition, we identified metabolic factors, such as the tryptophan di-dioxygenase TDO, for which we currently aim to understand how its inhibition protects against protein toxicity. We have recently developed a phenotypic screening pipeline and tools to motor both condensation and aggregation of disease proteins as well as their consequences for health and behavior. We are currently using this pipeline to uncover and understand the mechanisms involved in protein toxicity. Furthermore, we take advantage of our technology to explore how other systemic and environmental factors, such as neuronal circuits and microbiome-host interactions converge at such proteotoxic mechanisms.

THE FUTURE

We will continue our search for biological modifiers and their modes of action and, together with clinical and industrial partners, hope to find targets for interventions that protect or increase resilience to age-related protein toxicity.



A C. elegans worm expressing TDO tagged with a fluorescent marker (visible in pink)

Image credit: Anna Ainslie

SELECTED PUBLICATION

Stroo E, Janssen L, Sin O, Hogewerf W, Koster M, Harkema L, Youssef SA, Beschorner N, Wolters AH, Bakker B, Becker L, Garrett L, Marschall S, Hoelter SM, Wurst W, Fuchs H, Gailus-Durner V, Hrabe de Angelis M, Thathiah A, Foijer F, van de Sluis B, van Deursen J, Jucker M, de Bruin A, **Nollen EA**. Deletion of SERF2 in mice delays embryonic development and alters amyloid deposit structure in the brain. Life Sci Alliance. 2023 May 2;6(7): doi: 10.26508/lsa.202201730.

In age-related neurodegenerative diseases, like Alzheimer's and Parkinson's, disease-specific proteins become aggregation-prone and form amyloid-like deposits. Depletion of SERF proteins ameliorates this toxic process in worm and human cell models for diseases. Whether SERF modifies amyloid pathology in mammalian brain, however, has remained unknown. Here, we generated conditional Serf2 knockout mice and found that full-body deletion of Serf2 delayed embryonic development, causing premature birth and perinatal lethality. Brain-specific Serf2 knockout mice, on the other hand, were viable, and showed no major behavioral or cognitive abnormalities. In a mouse model for amyloid-β aggregation, brain depletion of Serf2 altered the binding of structure-specific amyloid dyes, previously used to distinguish amyloid polymorphisms in the human brain. These results suggest that Serf2 depletion changed the structure of amyloid deposits, which was further supported by scanning transmission electron microscopy, but further study will be required to confirm this observation. Altogether, our data reveal the pleiotropic functions of SERF2 in embryonic development and in the brain and support the existence of modifying factors of amyloid deposition in mammalian brain, which offer possibilities for polymorphism-based interventions.

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Liesbeth Veenhoff

CELLULAR BIOCHEMISTRY

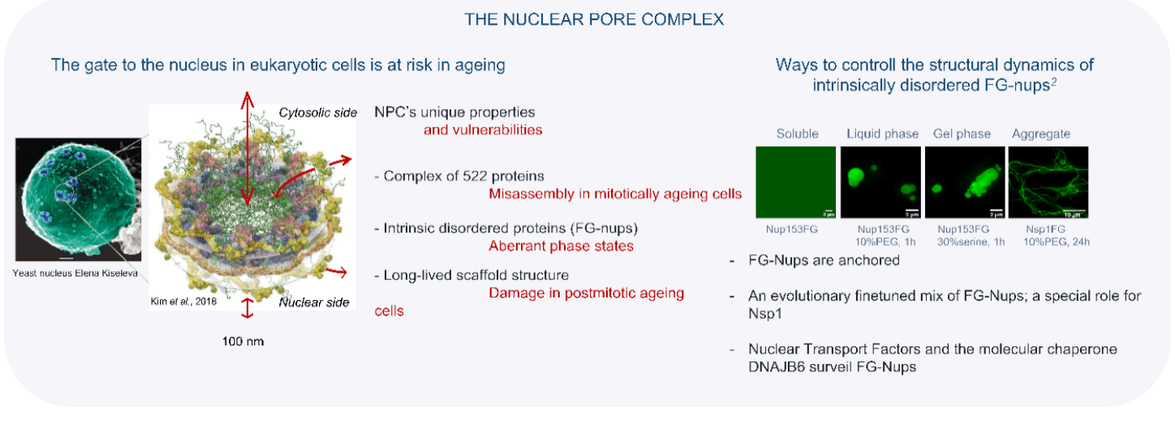
INTRODUCTION

The main research line in the group is to understand the role of the nuclear pore complex (NPC) in ageing. The NPCs are the sole gateways to the interior of the nucleus and their function is essential to all eukaryotic life. The NPC's function is intimately connected to the primary hallmarks of ageing of protein homeostasis and genome stability. We made contributions to the understanding of the structure and function of NPCs and in uncovering the vulnerabilities of NPCs in ageing cells. The surveillance of the intrinsically disordered proteins of the NPC is a main interest in the lab, as it appears that mechanisms that guard their structural state, also guard other intrinsically disordered proteins related to aggregation pathologies. This provides a new entry into the problem of protein aggregation pathologies and ageing. Complementing these studies aiming to uncover how the quality control of NPCs and intrinsically disordered proteins can be better safeguarded in ageing, we aim to contribute to a better understanding of the cellular ageing process in general.

RESEARCH FOCUS

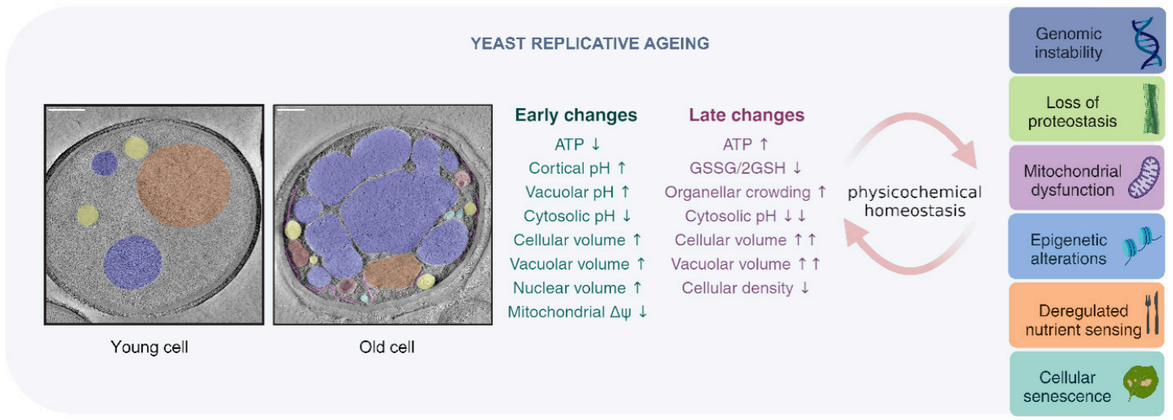
THE NUCLEAR PORE COMPLEX IN AGEING

The NPC's function is intimately connected to the primary hallmarks of ageing of proteins homeostasis and genome stability, and several processes underlying these hallmarks are orchestrated at NPCs. The NPC's function is compromised in ageing and age-related aggregation pathologies, and we aim to uncover the mechanisms responsible for NPC quality control.



THE PHYSICOCHEMICAL PERSPECTIVE ON CELLULAR AGEING

Cellular ageing described at the molecular level is a multifactorial process that leads to a spectrum of ageing trajectories. The function of all biological macromolecules depends on parameters such as pH, crowding, or redox state. We aim to contribute to the physicochemical homeostasis hypothesis of ageing by dissecting the influence of the intracellular milieu on molecular processes involved in ageing.



SELECTED PUBLICATION

Mouton, S. N., Boersma, A. J., & **Veenhoff, L. M**. (2023). A physicochemical perspective on cellular ageing. Trends in biochemical sciences, 48(11), 949–962. https://doi.org/10.1016/j.tibs.2023.08.007

Cellular ageing described at the molecular level is a multifactorial process that leads to a spectrum of ageing trajectories. There has been recent discussion about whether a decline in physicochemical homeostasis causes aberrant phase transitions, which are a driver of ageing. Indeed, the function of all biological macromolecules, regardless of their participation in biomolecular condensates, depends on parameters such as pH, crowding, and redox state. We expand on the physicochemical homeostasis hypothesis and summarise recent evidence that the intracellular milieu influences molecular processes involved in ageing.

THE FUTURE

We will continue to design our research from the viewpoint that studying "biology in time" is an unbiased way to reveal fundamental knowledge; knowledge that is needed to combat age-related diseases. Specifically, we aim to identify the proteins that detect damaged NPCs, to know the destiny of damaged NPCs, and to uncover the mechanisms that prevent damage to NPCs. Understanding how condensation of intrinsically disordered proteins is surveilled will also remain a main interest in the lab.Together, the planned research aims to uncover how the quality control of NPCs and intrinsically disordered proteins can be better safeguarded in ageing.

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John LaCava

MACROMOLECULES AND INTERACTOMES

INTRODUCTION

Our group has a specific technology focus: developing methods for interactome analyses. We specialize in affinity proteomic approaches. Presently, we aim to translate our research tools, which explore and characterize protein interactions within multi-component macromolecular complexes, towards the clinic: for example, identifying differences in protein complex constituents between healthy and diseased patient tissues. Several projects in the lab seek to apply our interactome analytical tools to diverse biological questions, typically (but not exclusively) with connections to human diseases. The characterization of human LINE-1 retrotransposons is central among our biological interests. Over evolutionary time, LINE-1 sequences have come to compose a large proportion of the human genome and the latest studies suggest clinical implications for LINE-1 expression in e.g., cancer, autoimmunity, and neurodegeneration. We continue to explore the roles of LINE-1 in colorectal cancers and systemic lupus erythematosus. Most recently, we have initiated studies into the emerging connections between LINE-1 and Alzheimer's disease.

RESEARCH FOCUS

Proteins and the multi-component macromolecular complexes they form are the effectors of cell biology. Studying cell biology therefore requires the ability to isolate distinct proteins along with other constituents of their associated macromolecules. Affinity proteomic techniques have greatly facilitated the discovery, purification, and characterization of endogenous protein complexes. These techniques leverage reagents able to target and capture proteins of interest assembled with physiological binding partners, from cell extracts. Although affinity capture has matured steadily as an approach, many technical shortcomings still limit its efficacy in the retrieval of intact, endogenous macromolecules. We address these challenges in affinity proteomics. We place special emphasis on approaches that also enable downstream structural and biochemical studies of enriched macromolecules. In the context of this technology focus, we are agnostic to the specific disease or underlying biology and collaborate widely on diverse projects with fundamental biologists and clinicians alike.

Long Interspersed Element 1 (LINE-1, L1), a retrotransposon, is a core biological interest of our lab. As a result of its "copy and paste" method of proliferation, L1 activity has contributed a large proportion of DNA to the human genome (including those sequences mobilized by L1, such as Alus). Since the insertion of new DNA sequences into the genome is inherently mutagenic, understanding the lifecycle of L1 is crucial to understanding human genome dynamics and cell biology. L1 DNA proliferates through an RNA intermediate whose protein products bind the L1 RNA to form a ribonucleoprotein (RNP) complex. L1 RNPs also co-opt and contend with a variety of host factors that facilitate or repress L1's ability to reach the chromatin and reintegrate into the genome. Thus, different subpopulations of L1 RNPs consist of different assortments of constituents, depending on the cell type, subcellular compartment, and on the pathway being traversed (proliferation or repression). Our goal is to expand our breadth of knowledge concerning the L1 interactome, and we study the structural and biochemical properties of L1 RNPs, considering these interactions. In doing so, we also explore L1 contributions to pathobiology.

THE FUTURE

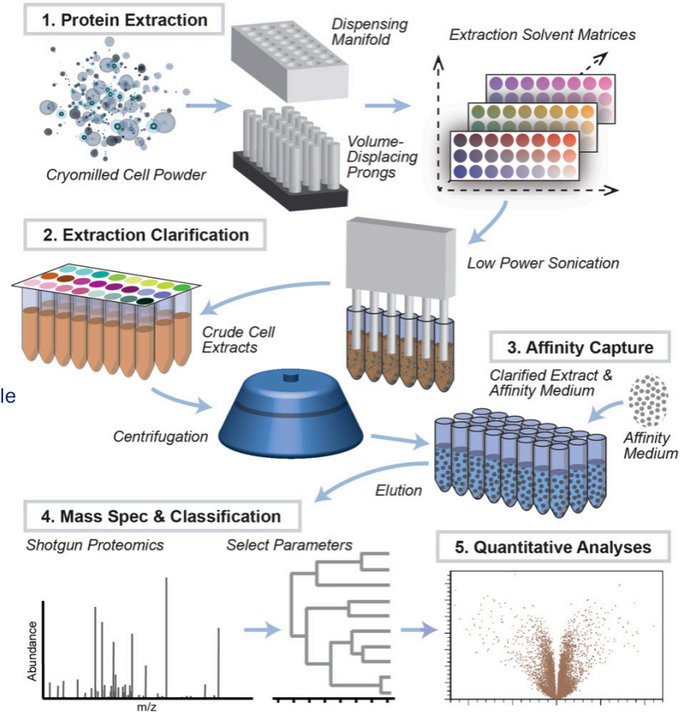
We are expanding our interactome charting approaches to include in situ proximity labeling. We will cross-reference macromolecular compositions defined by immunoprecipitation, which transfers macromolecules out of cells prior to identification, with those obtained by 'marking' the associating proteins while they still reside within cellular milieux. Taken together, the combination of these technique will provide complementary data to inform more comprehensive studies of protein complexes. We anticipate that proximity labeling may also allow us to make judicious use of FFPE tissue banks, whereas immunoprecipitation is carried out on fresh-frozen tissue, which is comparatively rare.

Our work with L1 is growing in numerous directions, chief among them, our development of a sensitive, quantitative biomarker assay for the detection of L1 ORF proteins in e.g., serum and cerebrospinal fluid. This assay is enabling us to explore diagnostic implications of L1 expression in cancers, autoimmunity, and neurodegeneration, which we are pursuing in on-going research.

SELECTED PUBLICATION

Baldwin ET, van Eeuwen T, Hoyos D, Zalevsky A, Tchesnokov EP, Sánchez R, Miller BD, Di Stefano LH, Ruiz FX, Hancock M, Işik E, Mendez-Dorantes C, Walpole T, Nichols C, Wan P, Riento K, Halls-Kass R, Augustin M, Lammens A, Jestel A, Upla P, Xibinaku K, Congreve S, Hennink M, Rogala KB, Schneider AM, Fairman JE, Christensen SM, Desrosiers B, Bisacchi GS, Saunders OL, Hafeez N, Miao W, Kapeller R, Zaller DM, Sali A, Weichenrieder O, Burns KH, Götte M, Rout MP, Arnold E, Greenbaum BD, Romero DL, **LaCava J**, Taylor MS. Structures, functions and adaptations of the human LINE-1 ORF2 protein. Nature.

The LINE-1 (L1) retrotransposon is an ancient genetic parasite that has written around one-third of the human genome through a 'copy and paste' mechanism catalysed by its multifunctional enzyme, open reading frame 2 protein (ORF2p)1. ORF2p reverse transcriptase (RT) and endonuclease activities have been implicated in the pathophysiology of cancer2,3, autoimmunity4,5 and ageing6,7, making ORF2p a potential therapeutic target. However, a lack of structural and mechanistic knowledge has hampered efforts to rationally exploit it. We report structures of the human ORF2p 'core' (residues 238–1061, including the RT domain) by X-ray crystallography and cryo-electron microscopy in several conformational states. Our analyses identified two previously undescribed folded domains, extensive contacts to RNA templates and associated adaptations that contribute to unique aspects of the L1 replication cycle. Computed integrative structural models of full-length ORF2p show a dynamic closed-ring conformation that appears to open during retrotransposition. We characterize ORF2p RT inhibition and reveal its underlying structural basis. Imaging and biochemistry show that non-canonical cytosolic ORF2p RT activity can produce RNA:DNA hybrids, activating innate immune signalling through cGAS/STING and resulting in interferon production6,7,8. In contrast to retroviral RTs, L1 RT is efficiently primed by short RNAs and hairpins, which probably explains cytosolic priming. Other biochemical activities including processivity, DNA-directed polymerization, non-templated base addition and template switching together allow us to propose a revised L1 insertion model. Finally, our evolutionary analysis demonstrates structural conservation between ORF2p and other RNA- and DNA-dependent polymerases. We therefore provide key mechanistic insights into L1 polymerization and insertion, shed light on the evolutionary history of L1 and enable rational drug development targeting L1



Methodological approach. Cryomilled cell powders are distributed with a dispensing manifold and macromolecules are extracted with different extraction solutions (1). Brief sonication is applied to disperse and homogenize the extracts (2). After clarifying the extracts by centrifugation, affinity capture is performed (3) and protein eluates are subjected to MS analysis (4) and data processing

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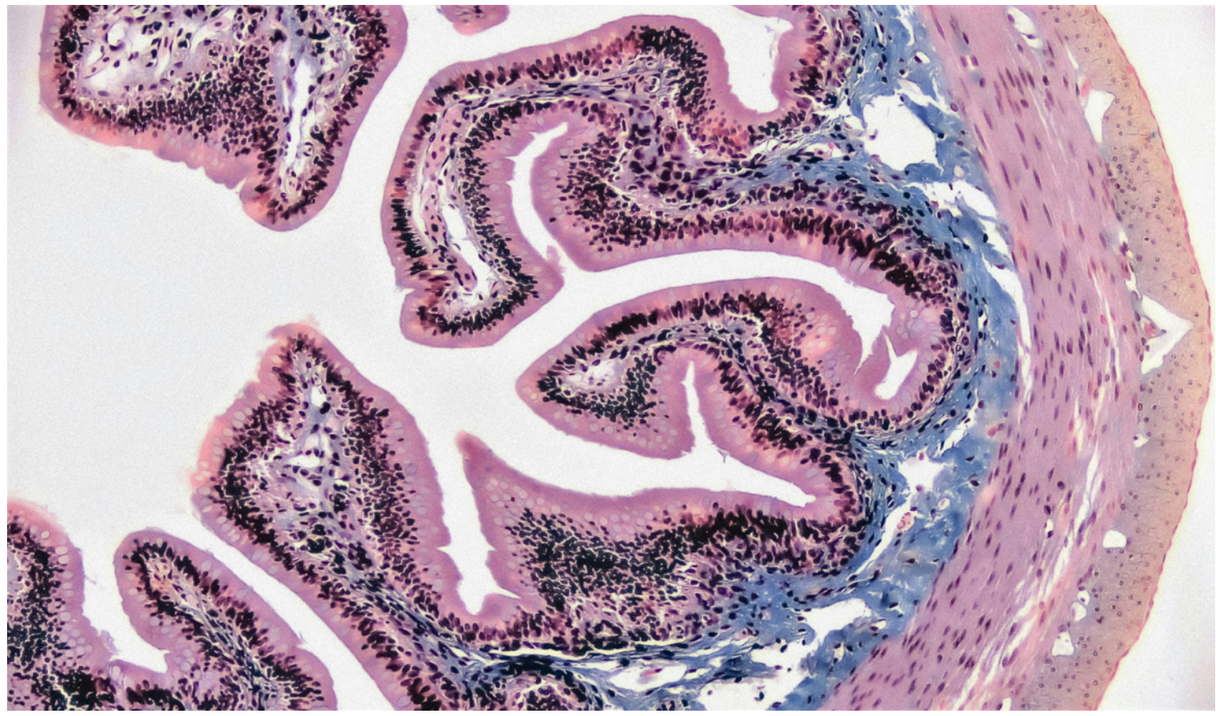
Mohammed Hanzala Post Doc
Joan Partes Internship Student
Anna O'Shea Internship Student
Aimee Pugh Internship Student
Jitze Snip Internship Student

Folkert Kuipers

LAB OF GUT-LIVER AXIS IN HEALTHY AGEING



The ageing process shows marked variability between individuals but also between different organs within an individual. This proposal focusses on the ageing liver, key in maintenance of whole body homeostasis. Therefore, age-related deterioration of liver functioning contributes to susceptibility to develop age-related diseases. Several hallmarks of ageing are known to impact on the different cell types of the liver. Yet, the factors that actually modulate ageing of the liver are unclear. Recent data indicates that metabolism of bile acids (BAs) is changed under conditions associated with increased life- and healthspan and, vice versa, that altered BA metabolism impacts human health. Primary BAs are formed in the liver and facilitate intestinal absorption of dietary fats. During their enterohepatic cycling, BAs interact with the gut microbiome leading to formation of secondary BAs. As a result, the human liver is exposed to a high (grams/day) load of differently structured BAs. It has been established in recent years that BAs also have hormone-like functions through activation nuclear and membrane-bound receptors involved in control of metabolic and inflammatory pathways as well as of detoxification reactions. Particularly secondary BAs have strong signalling capabilities. Our recent work has revealed great interindividual variability in BA pool composition in humans, related to genetic makeup of their microbiomes. Importantly, BAs have been associated with human longevity. Several new secondary BAs have been identified recently of which biological functions remain to be established. Using innovative mouse models with humanized BA metabolism, mechanisms of liver ageing will be identified and validated in a unique series of human liver biopsies, human donor livers on normothermic machine perfusion and liver-on-a-chip. Since the gut microbiome is amendable to manipulation, outcome of this work can contribute to new strategies to promote healthy (liver) ageing.

SELECTED PUBLICATION

Sjöland W, Wahlström A, Makki K, Schöler M, Molinaro A, Olsson L, Greiner TU, Caesar R, de Boer JF, **Kuipers F**, Bäckhed F, Marschall HU(2023) Absence of gut microbiota reduces neonatal survival and exacerbates liver disease in Cyp2c70-deficient mice with a human-like bile acid composition. Clinical Science

Chen L, Zhernakova DV, Kurilshikov A, Andreu-Sánchez S, Wang D, Augustijn HE, Vich Vila A, Lifelines Cohort Study, Weersma RK, Medema MH, Netea MG, **Kuipers F**, Wijmenga C, Zhernakova A, Fu J. (2022) Influence of the microbiome, diet and genetics on inter-individual variation in the human plasma metabolome. Nature Medicine.

Hendrix S, Kingma J, Ottenhoff R, Valiloo M, Svecla M, Zijlstra LF, Sachdev V, Kovac K, Levels JHM, Jongejan A, de Boer JF, **Kuipers F**, Rimbert A, Norata GD, Loregger A, Zelcer N. (2023) Hepatic SREBP signaling requires SPRING to govern systemic lipid metabolism in mice and humans. Nature Communications.

HIGHLIGHTS

This section reports a selected number of achievements that have been accomplished by ERIBA staff in 2022 and 2023.

GRADUATIONS

Thirteen students graduated from **ERIBA** in **2022** which include

Lin Zhou Foijer lab
Dhaozheng Yang de Haan Lab
Catalina Gaviria Agudelo Foijer Lab
Amanda Faria Assoni Foijer Lab
Nynke Talma Demaria Lab
Laura Jilderda Foijer Lab
Christy Hong Foijer Lab
Arthur Flohr Svendsen de Haan Lab
Hidde Zuidhox Cor Calkhoven Lab
Jamil Nehme Demaria Lab
Marije Semmelink Veenhoff Lab
Mandy Koopman Nollen Lab
Fernado Rosas Bringas Chang Lab.

Seven students successfully defended their PhD thesis in 2023 which include

Gloria Casas Gimeno Paridaen Lab
Tosca Martini de Haan Lab
Enikő Fekete-Szücs Chang Lab
Marlinde Smit De Haan & Bruggeman Lab
Eduardo Magalhaes Brugggeman Lab
Thamar Jessurun Lobo Guryev Lab
Elizabeth Riquelme Veenhoff Lab

GRANTS

ERIBA scientists were awarded with various prestigious grants.
The total funding for **2022** was **3.9 million** and in **2023** it was **4 million**.

PUBLICATIONS

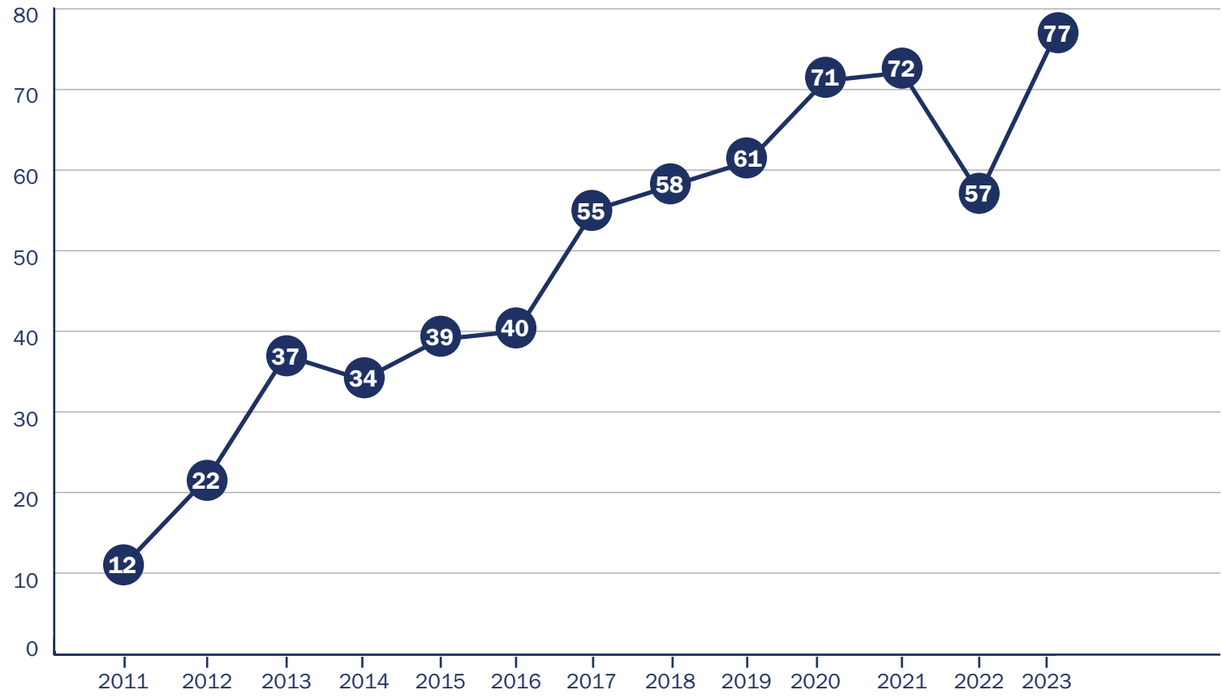
In **2022** ERIBA scientists published **57 papers** and in **2023 77 papers** were published.

AWARDS AND NOMINATIONS

In **2022** - **FSE** nominated the course that **Liesbeth Veenhoff** set up and am coordinating on the **molecular mechanisms of ageing and age-related diseases** for the '**best teaching practice award**' that the **RuG** gives out yearly. The course was selected out of all courses given within the FSE.

FACTS AND FIGURES

SCIENTIFIC PUBLICATIONS
FUNDING/GRANTS
PEOPLE
INVITED SPEAKERS



SCIENTIFIC PUBLICATIONS

SCIENTIFIC PUBLICATIONS 2022

57*

* **out of 57 papers 5 are pre-prints/online publications**

LABORATORY OF MOLECULAR NEUROBIOLOGY OF AGEING

Group Leader **Ellen Nollen**

Couzijn S, **Nollen EA.A** sudden collapse: the disaggregation of amyloid fibres. EMBO Journal.

Preprint
Wouter Huiting, Alejandra Duque-Jaramillo, Renée I. Seinstra, Harm. H. Kampinga, **Ellen A.A. Nollen**, Steven Bergink Preserving protein homeostasis prevents motor impairment in DNA Damage Response-compromised C. elegans. bioRxiv

LABORATORY OF ASYMMETRIC CELL DIVISION AND AGEING

Group Leader **Judith Paridaen**

Liang Y, Voshart D, **Paridaen JTML**, Oosterhof O, Liang D, Thiruvalluvan A, Zuhorn I, de Dunnen WFA, Zhang G, Lin H, Barazzuol L, Kruyt FAE (2022) CD146 increases stemness and aggressiveness in glioblastoma and activates YAP signaling. Cellular and Molecular Life Sciences.

Smit MJ , Martini TEI, Armandari I, Bockaj I, Zomerman WW, de Camargo Magalhães ES, Siragna Z, Meeuwsen TGJ, Scherpen FJG, Schoots M, Ritsema M, den Dunnen WFA, Hoving EW, **Paridaen JTML**, de Haan G, Guryev V, Bruggeman SWM. The developmental stage of the medulloblastoma cell-of-origin restricts Hedgehog pathway usage and drug sensitivity. Journal of Cell Science.

Casas Gimeno G, **Paridaen JTML**. (2022) The symmetry of neural stem and progenitor divisions in the vertebrate brain. Frontiers in Cell and Devlopmental Biology.

LABORATORY OF STEM CELL REGULATION AND MECHANISMS OF REGENERATION GROUP LEADER

Group Leader **Eugene Berezikov**

Genome assembly of the acoel flatworm Symsagittifera roscoffensis, a model for research on body plan evolution and photosymbiosis. Martinez P, Ustyantsev K, Biryukov M, Mouton S, Glasenburg L, Sprecher SG, Bailly X, **Berezikov E.**G3, Genes/Genomes/ Genetics.

MIig-SKP1 Gene Is Required for Spermatogenesis in the Flatworm Macrostomum lignano. Biryukov M, Dmitrieva A, Vavilova V, Ustyantsev K, Bazarova E, Sukhikh I, **Berezikov E**, Blinov A. International Journal of Mol Sciences.

Random Integration Transgenesis in a Free-Living Regenerative Flatworm Macrostomum lignano.Wudarski J, Ustyantsev K, Reinoite F, **Berezikov E**. Methods Molecular Biology.

LABORATORY OF GENE REGULATION IN AGEING AND AGE-RELATED DISEASES

Group Leader **Cor Calkhoven**

Sterken BA, Ackermann T, Müller C, Zuidhof HR, Kortman G, Hernandez-Segura A, Broekhuis M, Spierings D, Guryev V, **Calkhoven CF**. C/EBPβ isoform-specific regulation of migration and invasion in triple-negative breast cancer cells. NPJ Breast Cancer.

Müller C, Zidek LM, Eichwald S, Kortman G, Koster MH, **Calkhoven CF**.(2022) Enhanced C/EBPβ function promotes hypertrophic versus hyperplastic fat tissue growth and prevents steatosis in response to high-fat diet feeding. Elife.

Zuidhof HR, **Calkhoven CF**. (2022) Oncogenic and Tumor-Suppressive Functions of the RNA Demethylase FTO. Cancer Research.

LABORATORY OF CELLULAR SENESCENCE AND AGE-RELATED PATHOLOGIES

Group Leader **Marco Demaria**

Secomandi L, Borghesan M, Velarde M, **Demaria M.** (2022) The role of cellular senescence in female reproductive aging and the potential for senotherapeutic interventions. Human Reproduction Update.

Wang B, Varela-Eirin M, Brandenburg SM, Hernandez-Segura A, van Vliet T, Jongbloed EM, Wilting SM, Ohtani N, Jager A, **Demaria M**. (2022) Pharmacological CDK4/6 inhibition reveals a p53-dependent senescent state with restricted toxicity. EMBO Journal.

Varela-Eirín M, **Demaria M**.(2022) Cellular senescence. Current Biology.

Schmitt CA, Wang B, **Demaria M**. (2022) Senescence and cancer - role and therapeutic opportunities. Nature Reviews Clinical Oncology.

Malavolta M, Giacconi R, Piacenza F, Strizzi S, Cardelli M, Bigossi G, Marcozzi S, Tiano L, Marcheggiani F, Matacchione G, Giuliani A, Olivieri F, Crivellari I, Beltrami AP, Serra A, **Demaria M**, Provinciali M. Simple Detection of Unstained Live Senescent Cells with Imaging Flow Cytometry. Cells.

Domen A, Deben C, De Pauw I, Hermans C, Lambrechts H, Verswyvel J, Siozopoulou V, Pauwels P, **Demaria M**, van de Wiel M, Janssens A, Hendriks JMH, Van Schil P, Vermorken JB, Vandamme T, Prenen H, Peeters M, Lardon F, Wouters A. Prognostic implications of cellular senescence in resected non-small cell lung cancer. Translational Lung Cancer Research.

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Kohli J, Ge C, Fitsiou E, Doepner M, Brandenburg SM, Faller WJ, Ridky TW, **Demaria M**. (2022)Targeting anti-apoptotic pathways eliminates senescent melanocytes and leads to nevi regression. Nature Communications

Soto-Gamez A, Wang Y, Zhou X, Seras L, Quax W, **Demaria M**.(2022) Enhanced extrinsic apoptosis of therapy-induced senescent cancer cells using a death receptor 5 (DR5) selective agonist. Cancer Letters.

Preprint
Evangelou K, Vasileiou PV, Papaspyropoulos A, Hazapis O, Petty R, **Demaria M**, Gorgoulis VG. Cellular senescence and cardiovascular diseases: moving to the “heart” of the problem. Physiol Rev. 2022 Sep 1. doi: 10.1152/physrev.00007.2022. Online ahead of print. PMID: 36049114

LABORATORY OF TELOMERES AND GENOME INTEGRITY

Group Leader **Michael Chang**

Novarina D, Rosas Bringas FR, Rosas Bringas OG, **Chang M**. (2022) High-throughput replica-pinning approach to screen for yeast genes controlling low-frequency events. STAR Protocol.

Rosas Bringas FR, Stinus S, de Zoeten P, Cohn M, **Chang M**. (2022) Rif2 protects Rap1-depleted telomeres from MRX-mediated degradation in Saccharomyces cerevisiae. Elife.

Stinus S, Rosas Bringas FR, Wanders L, and **Chang M**. (2022) Investigating the role of G-quadruplexes at Saccharomyces cerevisiae telomeres. Microbial Cell.

Fekete-Szücs, E., Rosas Bringas, F.R., Stinus, S., and **Chang, M**. (2022) Suppression of cdc13-2¬-associated senescence by pif1-m2 requires Ku-mediated telomerase recruitment. G3.

LABORATORY OF CELLULAR BIOCHEMISTRY

Group Leader **Liesbeth Veenhof**

Wan Q, Mouton SN, **Veenhoff LM**, Boersma AJ. (2022) A FRET-based method for monitoring structural transitions in protein self-organization. Cell Reports Methods.

Kuiper EFE, Gallardo P, Bergsma T, Mari M, Kolbe Musskopf M, Kuipers J, Giepmans BNG, Steen A, Kampinga HH, **Veenhoff LM**, Bergink S.(2022) The chaperone DNAJB6 surveils FG-nucleoporins and is required for interphase nuclear pore complex biogenesis. Nature Cell Biology.

Preprint
Semmelink MFW, Jafarinia H, Wolters JC, Gheorghe T, Mouton SN, Steen A, Onck PR, **Veenhoff LM**. Nuclear transport under stress phenocopies transport defects in models of C9Orf72 ALS. bioRxiv

SEQUENCING FACILITY

Team Leader **Diana Spierings**

Tamminga M, Andree KC, van den Bos H, Hiltermann TJN, Mentink A, **Spierings DCJ**, Lansdorp P, Timens W, Schuuring E, Terstappen LWMM, Groen HJM. Leukapheresis increases circulating tumour cell yield in non-small cell lung cancer, counts related to tumour response and survival. British Journal of Cancer.

Gemble S, Wardenaar R, Keuper K, Srivastava N, Nano M, Macé AS, Tijhuis AE, Bernhard SV, **Spierings DCJ**, Simon A, Goundiam O, Hochegger H, Piel M, Foijer F, Storchová Z, Basto R. Author Correction: Genetic instability from a single S phase after whole-genome duplication. Nature.

Wu X, Ciminieri C, Bos IST, Woest ME, D'Ambrosi A, Wardenaar R, **Spierings DCJ**, Königshoff M, Schmidt M, Kistemaker LEM, Gosens R. Diesel exhaust particles distort lung epithelial progenitors and their fibroblast niche. Environmental Pollution.

Lubbers JM, Ważyńska MA, van Rooij N, Kol A, Workel HH, Plat A, Paijens ST, Vlaming MR, **Spierings DCJ**, Elsinga PH, Bremer E, Nijman HW, de Bruyn M.(2022) Expression of CD39 Identifies Activated Intratumoral CD8+ T Cells in Mismatch Repair Deficient Endometrial Cancer. Cancers.

Hanlon VCT, Chan DD, Hamadeh Z, Wang Y, Mattsson CA, **Spierings DCJ**, Coope RJN, Lansdorp PM. (2022) Construction of Strand-seq libraries in open nanoliter arrays. Cell Rep Methods.

Hong C, Schubert M, Tijhuis AE, Requesens M, Roorda M, van den Brink A, Ruiz LA, Bakker PL, van der Sluis T, Pieters W, Chen M, Wardenaar R, van der Vegt B, **Spierings DCJ**, de Bruyn M, van Vugt MATM, Foijer F.(2022) cGAS-STING drives the IL-6-dependent survival of chromosomally instable cancers. Nature.

Sterken BA, Ackermann T, Müller C, Zuidhof HR, Kortman G, Hernandez-Segura A, Broekhuis M, **Spierings D**, Guryev V, Calkhoven CF. (2022) C/EBPβ isoform-specific regulation of migration and invasion in triple-negative breast cancer cells. NPJ Breast Cancer.

Hintzen DC, Soto M, Schubert M, Bakker B, **Spierings DCJ**, Szuhai K, Lansdorp PM, Kluin RJC, Foijer F, Medema RH, Raaijmakers JA. (2022) The impact of monosomies, trisomies and segmental aneuploidies on chromosomal stability. PLoS One.

Bočkaj I, Martini TEI, Smit MJ, Armandari I, Bakker B, Wardenaar R, Meeuwsen-de Boer TGJ, Bakker PL, **Spierings DCJ**, Hoving EW, Guryev V, Foijer F, Bruggeman SWM. (2022) Chromosomal Instability Characterizes Pediatric Medulloblastoma but Is Not Tolerated in the Developing Cerebellum. International Journal Molecular Science.

Heijink AM, Stok C, Porubsky D, Manolika EM, de Kanter JK, Kok YP, Everts M, de Boer HR, Audrey A, Bakker FJ, Wierenga E, Tijsterman M, Guryev V, **Spierings DCJ**, Knipscheer P, van Boxtel R, Ray Chaudhuri A, Lansdorp PM, van Vugt MATM. (2022) Sister chromatid exchanges induced by perturbed replication can form independently of BRCA1, BRCA2 and RAD51. Nature Communications.

Shaikh N, Mazzagatti A, De Angelis S, Johnson SC, Bakker B, **Spierings DCJ**, Wardenaar R, Maniati E, Wang J, Boemo MA, Foijer F, McClelland SE. (2022) Replication stress generates distinctive landscapes of DNA copy number alterations and chromosome scale losses. Genome Biology.

Mañas A, Aaltonen K, Andersson N, Hansson K, Adamska A, Seger A, Yasui H, van den Bos H, Radke K, Esfandyari J, Bhave MS, Karlsson J, **Spierings D**, Foijer F, Gisselsson D, Bexell D. Clinically relevant treatment of PDX models reveals patterns of neuroblastoma chemoresistance. Science Advances.

LABORATORY OF GENOMIC INSTABILITY IN DEVELOPMENT AND DISEASE

Group Leader **Floris Foijer**

Gemble S, Wardenaar R, Keuper K, Srivastava N, Nano M, Macé AS, Tijhuis AE, Bernhard SV, Spierings DCJ, Simon A, Goundiam O, Hochegger H, Piel M, **Foijer F**, Storchová Z, Basto R. (2022) Author Correction: Genetic instability from a single S phase after whole-genome duplication. Nature.

Eerkens AL, Vledder A, van Rooij N, **Foijer F**, Nijman HW, de Bruyn M. (2022) Rapid and efficient generation of antigen-specific isogenic T cells from cryopreserved blood samples. Immunology and Cell Biology.

Bockaj I, Martini TEI, Smit MJ, Armandari I, Bakker B, Wardenaar R, Meeuwsen-de Boer TGJ, Bakker PL, Spierings DCJ, Hoving EW, Guryev V, **Foijer F** and Bruggeman SWM. (2022) Chromosomal Instability Characterizes Pediatric Medulloblastoma but Is Not Tolerated in the Developing Cerebellum International Journal of Molecular Sciences.

Klaasen SJ, Truong MA, van Jaarsveld RH, Koprivec I, Štimac V, de Vries SG, Risteski P, Kodba S, Vukušić K, de Luca K, Marques JF, Gerrits EM, Bakker B, **Foijer F,** Kind J, Tolić IM, Lens SMA and Kops GJPL.(2022) Nuclear position of chromosomes dictates probability of missegregation and micronuclear entrapment. Nature.

Hong C, Schubert M, Tijhuis AE, Requesens M, Roorda M, van den Brink A, Andrade Ruiz L, Bakker PL, van der Sluis T, Pieters W, Chen M, Wardenaar R, van der Vegt B, Spierings DCJ, de Bruyn M, van Vugt MATM, and **Foijer F**.(2022) IL6 signalling as a targetable vulnerability in chromosomally instable cancers. Nature.

Hintzen DC, Soto M., Schubert M., Bakker B., Spierings DCJ, Szuhai K., Lansdorp PM, **Foijer F**, Medema RH, Raaijmakers JA. Monosomies, trisomies and segmental aneuploidies differentially affect chromosomal stability. PLOS One.

Shaikh N, Mazzagatti A, De Angelis S, Johnson SC, Bakker B, Spierings DCJ, Wardenaar R, Maniati E, Wang J, Boemo MA, **Foijer F,** McClelland SE.(2022) Replication stress generates distinctive landscapes of DNA copy number alterations and chromosome scale losses. Genome Biology.

Assoni AF, **Foijer F**, Zatz M.(2022) Amyotrophic Lateral Sclerosis, FUS and Protein Synthesis Defects. Stem Cell Reviews and Reports.

Mañas A, Aaltonen K, Andersson N, Hansson K, Adamska A, Seger A, Yasui H, van den Bos H, Radke K, Esfandyari J, Bhave MS, Karlsson J, Spierings D, **Foijer F**, Gisselsson D, Bexell D. Clinically relevant treatment of PDX models reveals patterns of neuroblastoma chemoresistance. Sciences Advances.

LABORATORY OF GENOME STRUCTURE AGEING

Group Leader **Victor Guryev**

van der Kamp MF, Halmos GB, **Guryev V**, Horvatovich PL, Schuuring E, van der Laan BFAM, van der Vegt B, Plaat BEC, Verhoeven CJ. (2022) Age-specific oncogenic pathways in head and neck squamous cell carcinoma - are elderly a different subcategory? Cellular Oncology.

Zverinova S, **Guryev V**. (2022) Variant calling: Considerations, practices, and developments. Human Mutation.

Bočkaj I, Martini TEI, Smit MJ, Armandari I, Bakker B, Wardenaar R, Meeuwsen-de Boer TGJ, Bakker PL, Spierings DCJ, Hoving EW, **Guryev V**, Foijer F, Bruggeman SWM. Chromosomal Instability Characterizes Pediatric Medulloblastoma but Is Not Tolerated in the Developing Cerebellum. International Journal Molecular Science.

Smit MJ, Martini TEI, Armandari I, Bočkaj I, Zomerman WW, de Camargo Magalhães ES, Siragna Z, Meeuwsen TGJ, Scherpen FJG, Schoots MH, Ritsema M, den Dunnen WFA, Hoving EW, Paridaen JTML, de Haan G, **Guryev V**, Bruggeman SWM. The developmental stage of the medulloblastoma cell-of-origin restricts Sonic hedgehog pathway usage and drug sensitivity. Journal of Cell Science.

Naslavsky MS, Scliar MO, Yamamoto GL, Wang JYT, Zverinova S, Karp T, Nunes K, Ceroni JRM, de Carvalho DL, da Silva Simões CE, Bozoklian D, Nonaka R, Dos Santos Brito Silva N, da Silva Souza A, de Souza Andrade H, Passos MRS, Castro CFB, Mendes-Junior CT, Mercuri RLV, Miller TLA, Buzzo JL, Rego FO, Araújo NM, Magalhães WCS, Mingroni-Netto RC, Borda V, Guio H, Rojas CP, Sanchez C, Caceres O, Dean M, Barreto ML, Lima-Costa MF, Horta BL, Tarazona-Santos E, Meyer D, Galante PAF, **Guryev V**, Castelli EC, Duarte YAO, Passos-Bueno MR, Zatz M.(2022) Whole-genome sequencing of 1,171 elderly admixed individuals from São Paulo, Brazil. Nature Communications.

Sterken BA, Ackermann T, Müller C, Zuidhof HR, Kortman G, Hernandez-Segura A, Broekhuis M, Spierings D, **Guryev V**, Calkhoven CF.(2022) C/EBPβ isoform-specific regulation of migration and invasion in triple-negative breast cancer cells. NPJ Breast Cancer.

Ditz B, Boekhoudt J, Couto N, Brandsma CA, Hiemstra PS, Tew GW, Neighbors M, Grimbaldeston MA, Timens W, Kerstjens HAM, Rossen JWA, **Guryev** V, van den Berge M, Faiz A. (2022)The Microbiome in Bronchial Biopsies from Smokers and Ex-Smokers with Stable COPD - A Metatranscriptomic Approach. COPD: Journal of Chronic obstrutive pulmonary Disease.

Hagemeijer YP, **Guryev V**, Horvatovich P. (2022) Accurate Prediction of Protein Sequences for Proteogenomics Data Integration. Methods Molecular Biology.

Heijink AM, Stok C, Porubsky D, Manolika EM, de Kanter JK, Kok YP, Everts M, de Boer HR, Audrey A, Bakker FJ, Wierenga E, Tijsterman M, **Guryev V**, Spierings DCJ, Knipscheer P, van Boxtel R, Ray Chaudhuri A, Lansdorp PM, van Vugt MATM.(2022) Sister chromatid exchanges induced by perturbed replication can form independently of BRCA1, BRCA2 and RAD51. Nature Communications.

Hanlon VCT, Lansdorp PM, **Guryev V**. (2022) A survey of current methods to detect and genotype inversions. Human Mutations.

Bernal V, Soancatl-Aguilar V, Bulthuis J, **Guryev V**, Horvatovich P, Grzegorczyk M. (2022) GeneNetTools: tests for Gaussian graphical models with shrinkage. Bioinformatics.

LABORATORY OF MACROMOLECULES AND INTERACTOMES

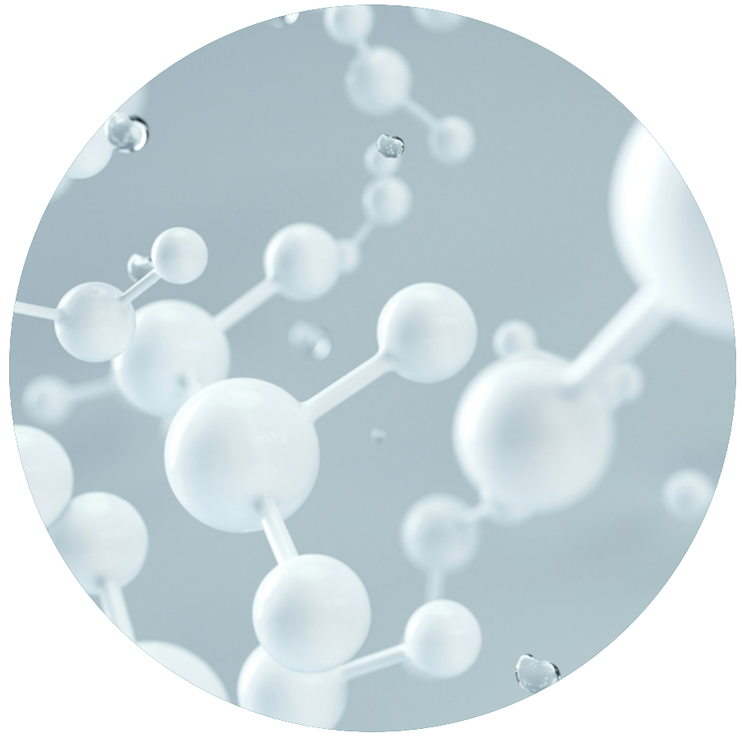
Group Leader **John LaCava**

McKerrow W, Wang X, Mendez-Dorantes C, Mita P, Cao S, Grivainis M, Ding L, **LaCava J,** Burns KH, Boeke JD, Fenyö D.(2022) LINE-1 expression in cancer correlates with p53 mutation, copy number alteration, and S phase checkpoint. Proceedings of the National Academic of Science.

Huiting W, Dekker SL, van der Lienden JCJ, Mergener R, Musskopf MK, Furtado GV, Gerrits E, Coit D, Oghbaie M, Di Stefano LH, Schepers H, van Waarde-Verhagen MAWH, Couzijn S, Barazzuol L, **LaCava J**, Kampinga HH, Bergink S. (2022)Targeting DNA topoisomerases or checkpoint kinases results in an overload of chaperone systems, triggering aggregation of a metastable subproteome. Elife.

Preprint
Affinity-Based Interactome Analysis of Endogenous LINE-1 Macromolecules.

Di Stefano LH1, Saba LJ1, Oghbaie M2, Jiang H2, McKerrow W3, Benitez-Guijarro M4, Taylor MS5, **LaCava J**1. In M.R. Branco & A. de Mendoza Soler (Eds.), Transposable Elements: Methods and Protocols. Springer. DOI: 10.1007/978-1-0716-2883-6_12



LABORATORY OF GUT-LIVER AXIS IN HEALTHY AGEING

Group Leader **Folkert Kuipers**

Doestzada M, Zhernakova DV, van den Munckhof ICL, Wang D, Kurilshikov A, Chen L, Bloks VW, van Faassen M, Rutten JHW, Joosten LAB, Netea MG, Wijmenga, CW, Riksen NP, Zhernakova A, **Kuipers F,** Fu J. (2022) Systematic analysis of relationships between plasma branched-chain amino acid concentrations and cardiometabolic parameters: an association and Mendelian randomization study. BMC Medicine.

Chen L, Zhernakova DV, Kurilshikov A, Andreu-Sánchez S, Wang D, Augustijn HE, Vich Vila A, Lifelines Cohort Study, Weersma RK, Medema MH, Netea MG, **Kuipers F**, Wijmenga C, Zhernakova A, Fu J. (2022) Influence of the microbiome, diet and genetics on inter-individual variation in the human plasma metabolome. Nature Medicine.

Meijnikman AS, van Olden CC, Aydin, Herrema H, Kaminska D, Lappa D, Männistö V, Tremaroli V, Olofsson LE, de Brauw M, van de Laar A, Verheij J, Gerdes VEA, Schwartz TW, Nielsen J, Bäckhed F, Pajukanta P, Philajamäki J, Tchkonia T, Kirkland JL, **Kuipers F**, Nieuwdorp M, Groen AK.(2022) Hyperinsulinemia is highly associated with hepatocytic senescence in two independent cohorts. Diabetes.

Preprint

J. Yang, H.D. de Vries, A. Mayeuf-Louchart, J.H. Stroeve, V.W. Bloks, M. Koehorst, H. Duez, B. Staels, **F. Kuipers**, T. van Zutphen. Role of bile acid signalling via FXR in development and function of brown adipose tissue. BBA-Mol Cell Biol Lipids 1868(2):159257, 2023 doi: 10.1016/j.bbalip.2022.159257

Patent pending

Walt, DR, C Wu, L Cohen, P Garden, K Burns, M Taylor, PC Fridy, BT Chait, KR Molloy, MP Rout, & **JP LaCava**. Ultrasensitive Assays for Detection of ORF1p in Biofluids. U.S. Patent Application No. 63/423,696. 2022

SCIENTIFIC PUBLICATIONS 2023

77*

* **out of 77 papers 6 are pre-prints/online publications**

LABORATORY OF MOLECULAR NEUROBIOLOGY OF AGEING

Group Leader **Ellen Nollen**

Koopman M, Güngördü L, Seinstra RI, **Nollen EAA** 1(2023) Neuronal overexpression of hTDP-43 in Caenorhabditis elegans impairs motor function. microPubli Bio.

Koopman M, Güngördü L , Seinstra RI, Hogewerf W, **Nollen EAA** (2023) Neuronal overexpression of hTDP-43 in Caenorhabditis elegans mimics the cellular pathology commonly observed in TDP-43 proteinopathies. MicroPubl Biol.

Koopman M, Güngördü L, Seinstra RI, **Nollen EAA** (2023) Neuronal overexpression of hTDP-43 in Caenorhabditis elegans impairs different neuronally controlled behaviors and decreases fecundity. MicroPublication Biology.

Koopman M, Güngördü L, Seinstra RI, **Nollen EAA** (2023) Neuronal overexpression of human TDP-43 in Caenorhabditis elegans causes a range of sensorimotor phenotypes. MicroPublication Biology.

Stroo E, Janssen L, Sin O, Hogewerf W, Koster M, Harkema L, Youssef SA , Beschorner N,Wolters AHG, Bakker B, Becker L, Garrett L, Marschall S, Hoelter SM, Wurst W, Fuchs H, Gailus-Durner V, Hrabe de Angelis M, Thathiah A, Foijer F, van de Sluis B, van Deursen J, Jucker M, de Bruin A, **Nollen EAA**. (2023) Deletion of SERF2 in mice delays embryonic development and alters amyloid deposit structure in the brain. Life Science Alliance.

Preprint

Mandy Koopman, Lale Güngördü, Leen Janssen, Renée I. Seinstra, Janet E. Richmond, Nathan Okerlund, René Wardenaar, Priota Islam, Andre E.X. Brown, Erik M. Jorgensen, **Ellen A.A. Nollen**

Rebalancing the motor circuit restores movement in a Caenorhabditis elegans model for TDP-43- toxicity doi: https://doi.org/10.1101/2023.10.24.563563

LABORATORY OF MACROMOLECULES AND INTERACTOMES

Group Leader **John LaCava**

Di Stefano LH, Saba LJ, Oghbaie M, Jiang H, McKerrow W, Benitez-Guijarro M, Taylor MS, **LaCava J.** (2023) Affinity-Based Interactome Analysis of Endogenous LINE-1 Macromolecules. Methods Mol Biol.

Xie S, Bu C, **LaCava J,** Chi L (2023) MsPHep: An online application for low molecular weight heparin rapid characterization based on liquid chromatography-tandem mass spectrometry. J Chromatogr A.

Expression of L1 retrotransposons in granulocytes from patients with active systemic lupus erythematosus (2023) Ukadike KC , Najjar R, Ni K , Laine A , Wang X , Bays A , Taylor MS, **LaCava J**, Mustelin T. Mob DNA.

Taylor MS, Wu C, Fridy PC, Zhang SJ, Senussi Y, Wolters JC, Cajuso T, Cheng WC, Heaps JD, Miller BD, Mori K, Cohen L, Jiang H, Molloy KR, Chait BT, Goggins MG, Bhan I, Franses JW, Yang X, Taplin ME, Wang X, Christiani DC, Johnson BE, Meyerson M, Uppaluri R, Egloff AM, Denault EN, Spring LM, Wang TL, Shih IM, Fairman JE, Jung E, Arora KS, Yilmaz OH, Cohen S, Sharova T, Chi G, Norden BL, Song Y, Nieman LT, Pappas L, Parikh AR, Strickland MR, Corcoran RB, Mustelin T, Eng G, Yilmaz ÖH, Matulonis UA, Chan AT, Skates SJ, Rueda BR, Drapkin R, Klempner SJ, Deshpande V, Ting DT, Rout MP, **LaCava J**, Walt DR, Burns KH. Ultrasensitive Detection of Circulating LINE-1 ORF1p as a Specific Multicancer Biomarker. Cancer Discovery.

Baldwin ET, van Eeuwen T, Hoyos D, Zalevsky A, Tchesnokov EP, Sánchez R, Miller BD, Di Stefano LH, Ruiz FX, Hancock M, Işik E, Mendez-Dorantes C, Walpole T, Nichols C, Wan P, Riento K, Halls-Kass R, Augustin M, Lammens A, Jestel A, Upla P, Xibinaku K, Congreve S, Hennink M, Rogala KB, Schneider AM, Fairman JE, Christensen SM, Desrosiers B, Bisacchi GS, Saunders OL, Hafeez N, Miao W, Kapeller R, Zaller DM, Sali A, Weichenrieder O, Burns KH, Götte M, Rout MP, Arnold E, Greenbaum BD, Romero DL, **LaCava J**, Taylor MS. Structures, functions and adaptations of the human LINE-1 ORF2 protein. Nature.

Preprint

Sun S, Hong J, You E, Tsanov KM, Chacon-Barahona J, Gioacchino AD, Hoyos D, Li H, Jiang H, Ly H, Marhon S, Murali R, Chanda P, Karacay A, Vabret N, De Carvalho DD, **LaCava** J, Lowe SW, Ting DT, Iacobuzio-Donahue CA, Solovyov A, Greenbaum BD. (2023) Cancer cells co-evolve with retrotransposons to mitigate viral mimicry.

LABORATORY OF STEM CELL REGULATION AND MECHANISMS OF REGENERATION GROUP LEADER

Group Leader **Eugene Berezikov**

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LABORATORY OF ASYMMETRIC CELL DIVISION AND AGEING

Group Leader **Judith Paridaen**

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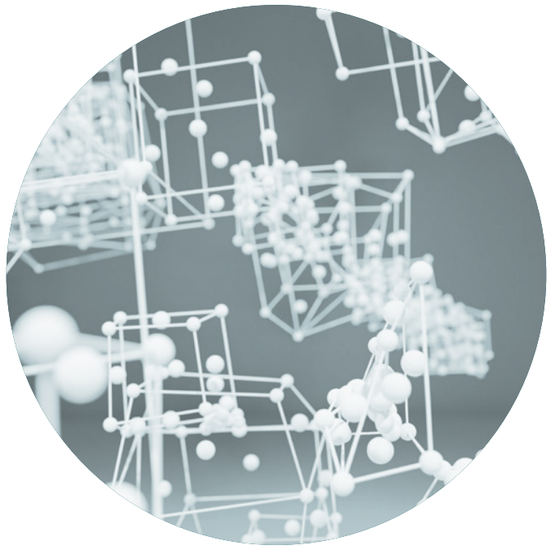

LABORATORY OF GENE REGULATION IN AGEING AND AGE-RELATED DISEASES

Group Leader **Cor Calkhoven**

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LABORATORY OF CELLULAR SENESCENCE AND AGE-RELATED PATHOLOGIES

Group Leader **Marco Demaria**

Magkouta S, Veroutis D, Pousias A, Papaspyropoulos A, Pippa N, Lougiakis N, Kambas K, Lagopati N, Polyzou A, Georgiou M, Chountoulesi M, Pispas S, Foutadakis S, Pouli N, Marakos P, Kotsinas A, Verginis P, Valakos D, Mizi A, Papantonis A, Vatsellas G, Galanos P, Bartek J, Petty R, Serrano M, Thanos D, Roussos C, **Demaria M**, Evangelou K, Gorgoulis VG. (2023) A fluorophore-conjugated reagent enabling reapid detection, isolation and live tracking of senescent cells. Molecular Cell.

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LABORATORY OF TELOMERES AND GENOME INTEGRITY

Group Leader **Michael Chang**

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LABORATORY OF CELLULAR BIOCHEMISTRY

Group Leader **Liesbeth Veenhof**

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Team Leader **Diana Spierings**

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LABORATORY OF GENOMIC INSTABILITY IN DEVELOPMENT AND DISEASE

Group Leader **Floris Foijer**

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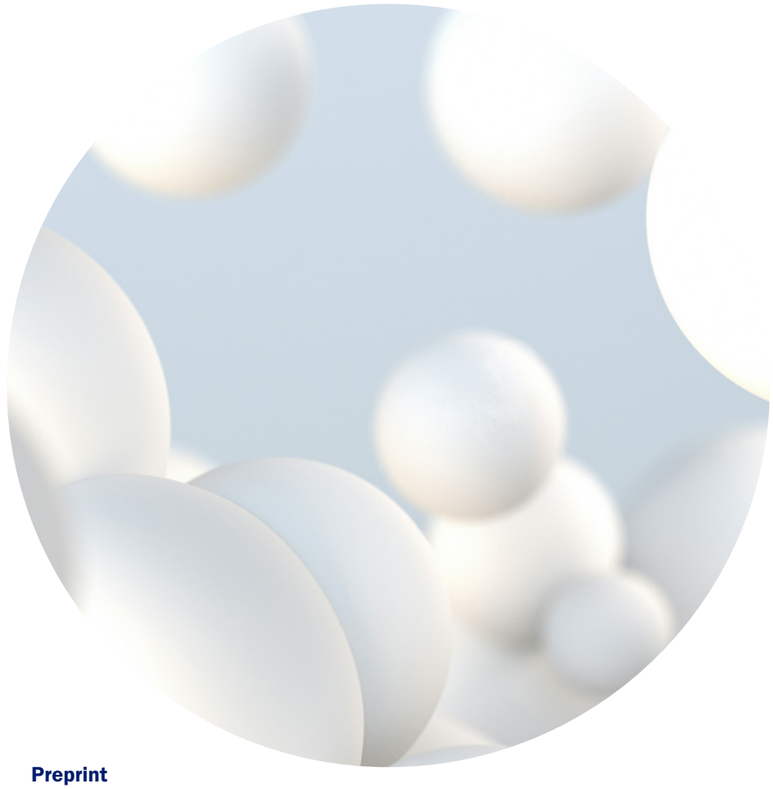

LABORATORY OF GENOME STRUCTURE AGEING

Group Leader **Victor Guryev**

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LABORATORY OF GUT-LIVER AXIS IN HEALTHY AGEING

Group Leader **Folkert Kuipers**

Martens N, Zhan NA, Voortman G, Leijten FPJ, van Rheenen C, van Leerdam S, Geng X, Huybrechts M, Liu H, Jonker JW, **Kuipers F**, Lütjohann D, Vanmierlo T, Mulder MT (2023) Activation of Liver X Receptors and Peroxisome Proliferator-Activated Receptors by Lipid Extracts of Brown Seaweeds: A Potential Application in Alzheimer's Disease? Nutrients.

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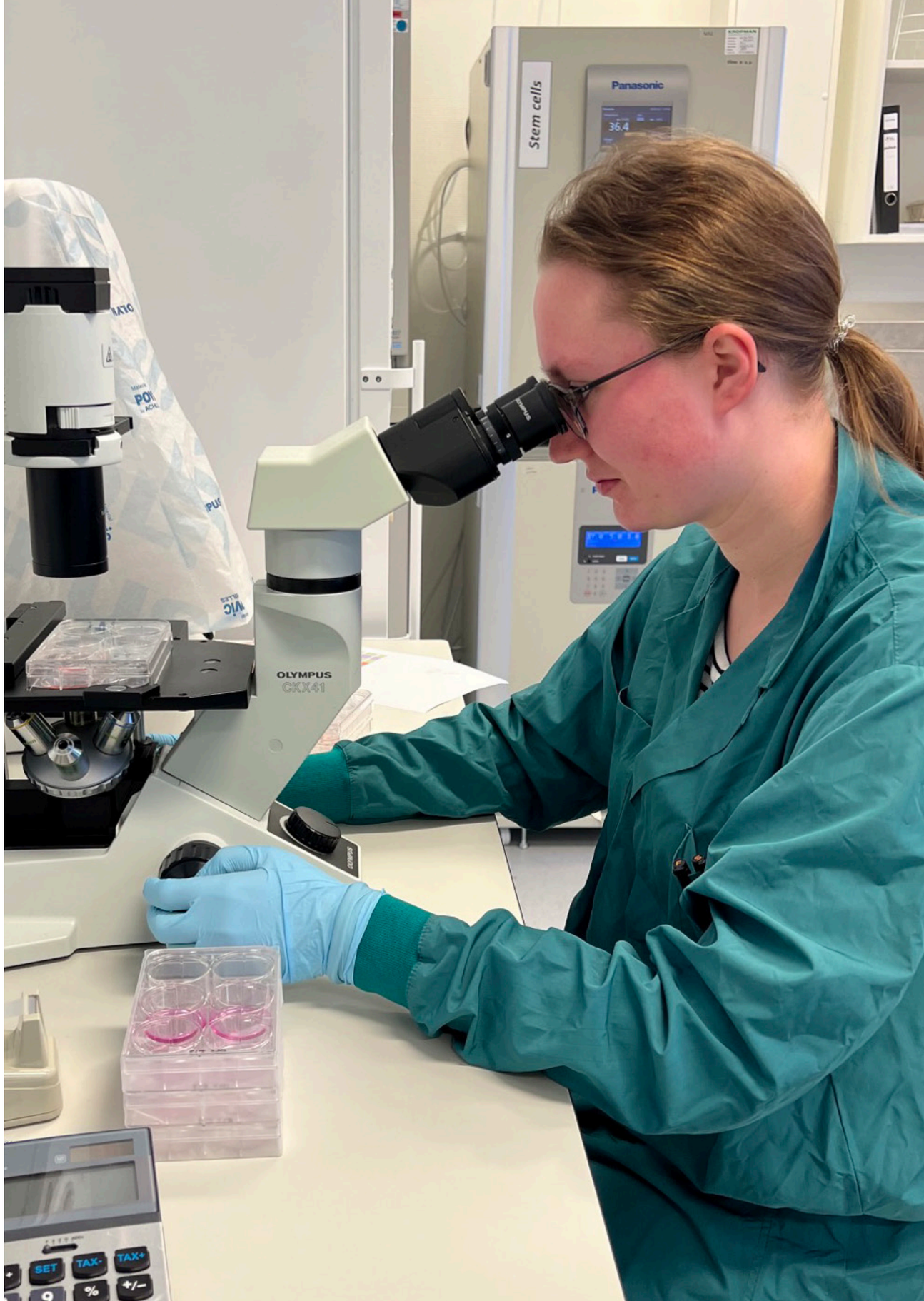


FUNDING/GRANTS 2022 €3,9M

Researcher	Call	Title of the Project	Budget
Ellen Nollen	SRA Merck Sharp & Dohme Corp.	Using C.elegans worms to investigate KP-related neuroprotection by TDO inhibition	€602,188
Ellen Nollen	PPP Merck Sharp & Dohme Corp. + ALS Nederland	Using C.elegans worms to investigate KP-related neuroprotection by TDO inhibition	€767,300
Eugene Berezikov	MSCA-Doctoral Networks Horizon Europe	REGENERATE-IT	€613,346
Marco Demaria	KWF Grant	Targeting cellular senescence to alleviate anthracyclines-induced toxicity	€776,028
Eugene Berezikov	NWO Open Competition Domain Science – XS	“Identification of proteins that protect DNA during extreme environmental conditions in diapaused killifish embryos and investigation of their application potential in human”	€50,000
Marco Demaria	KRF 2022-1	Acquisition of an oxygen regulator for rodents to study how exposure to hypoxia reduces senescence-driven chemotoxicity	€42,350
John LaCava	SRA RibonTx	Close the loop between PARP14 function in vivo and in vitro	€75,000
John LaCava	Lupus Research Alliance -Global Team Science Award	IFN-I-dependent lupus is caused by pathogenic nucleic acids	€10,000
Daniele Novarina (Michael Chang)	NWO Open Competition Domain Science - XS	A novel approach to identify genetic regulators of prion formation	€50,000
Kirill Ustyantsev (Eugene Berezikov)	NWO Open Competition Domain Science - XS	A universal, adaptable, and non-toxic method to treat resistant parasitic flatworm and roundworm infections	€50,000
Maria Suarez (Floris Foijer)	Marie Skłodowska-Curie Actions – Postdoctoral Fellowships	Revealing genes that mediate the CIN-induced interferon-inflammatory response using a Genome-wide CRISPR screen coupled to a Suicide Gene Switch	€187,000
Siqi Zheng (Floris Foijer)	De Cock-Hadders	The roles of extracellular vesicles in chromosomally unstable cells	€4,000
Anne de Groot (Gerald de Haan)	De Cock-Hadders	Characterizing the dualistic role of CBX7 on leukemic cell proliferation	€4,000

€3,992,112

FUNDING/GRANTS 2023 €4,1M

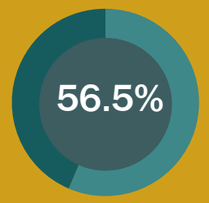
PI	Call	Title	Budget
Eugenia Goya (Ellen Nollen)	Parkinsonfonds	a fast testing platform to study the effect of single bacterial species from the gut microbiota in C.elegans models of Parkinson’s Disease	€93,174
Floris Foijer	NWO-VICI	How do chromosomal unstable tumours escape immune surveillance?	€1,500,000
Chen Ge (Marco Demaria)	De Cock-Hadders	UVB-induced senescence in the skin and role in melanomagenesis	€4,500
Myrthe Klaver (Marco Demaria)	De Cock-Hadders	Cellular senescence refers to a cell state of irreversible cell cycle arrest	€4,500
Anne de Groot (Gerald de Haan)	De Cock-Hadders	Characterizing the dualistic role of CBX7 on leukemic cell proliferation.	€4,000
Marco Demaria	Hevolution /AFAR New Investigator Award	Targeting altered Ca2+ signaling in cellular senescence to extend healthy longevity	€375,000
John LaCava	Kenneth Rainin Foundation	Understanding the role of lysosomal autophagy in inflammatory bowel disease”	€79,546
Cor Calkhoven	NWO_Conference grant	Groningen Jena Aging Meeting	€15,000
John LaCava	SRA Ribon TX	PARP14 interactomes in disease: close the loop between PARP14 function in vivo and in vitro”	€310,000
John LaCava	PPP Ribon Tx	PARP14 interactomes in disease: close the loop between PARP14 function in vivo and in vitro”	€380,000
Paola (Liesbeth Veenhoff)	NWO-XS	Preventing proteins from sticky situations	€50,000
Floris Foijer	Lymph&Co.	Exploiting chromosomal instability-induced cancer cell inflammation to treat lymphoma	€698,877
Marco Demaria	ONO Pharma PPP	Identification of detrimental functions of senescent cells in human diseases	€543,000

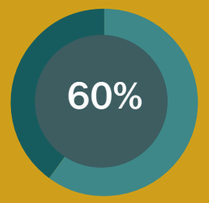
€4,057,597

PEOPLE

2022

EMPLOYEES
92

STAFF UNDER 40


FEMALE EMPLOYEES


NUMBER OF NATIONALITIES
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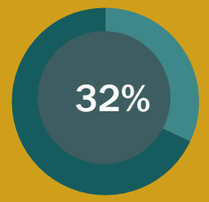
INTERNATIONALS


MALE EMPLOYEES
37

DOCTORAL STUDENTS EMPLOYED BY ERIBA
38

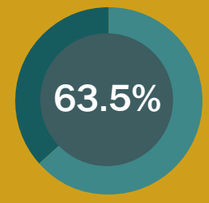
DOCTORAL STUDENTS HOSTED BY ERIBA UNDER THE GSMS BURSARY SCHEME


Management team ERIBA

Folkert Kuipers Head of Department/ Scientific Director
Henk Heidekamp Managing Director
Ria Ubels Staff Advisor
Megha Upadhyay Research Coordinator
Kevin Huizinga Financial controller
Sylvia Hoks Secretary
Karin van Wageningen Secretary
Joke Eleveld Secretary
Yin Fai Chan Technician (general support)

2023

EMPLOYEES
85

STAFF UNDER 40


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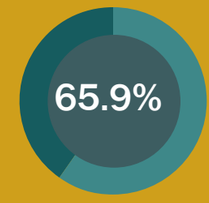
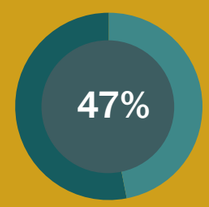


NUMBER OF NATIONALITIES
26

INTERNATIONALS


MALE EMPLOYEES
29

DOCTORAL STUDENTS EMPLOYED BY ERIBA
39

DOCTORAL STUDENTS HOSTED BY ERIBA UNDER THE GSMS BURSARY SCHEME


INVITED SPEAKERS 2022

Date	External Invited Speaker	Host	Title of the talk	Institute	Event
2/12/2022	Marit Westerterp	Folkert Kuipers	Cholesterol efflux pathways control T cell aging and atherosclerosis	University Medical Center Groningen	ERIBA Friday Seminar
16/6/2022	Omar Yilmaz	John LaCava	Dietary Control of Stem Cells in Physiology and Disease	Koch Institute for Integrative Cancer Research at MIT and Massachusetts General Hospital and Harvard Medical School	ERIBA Friday Seminar
23/09/2022	Kas Houthuijs	John LaCava	The BioHack Academy and the importance to have artists and designers working together with scientists on new (bio)technologies	Waag Futurelab	ERIBA Friday Seminar
23/09/2022	Lucas Evers	John LaCava	TBD/never received	Waag Futurelab	ERIBA Friday Seminar
01/11/2022	Mario Niepel	John LaCava	PARP14 as Pharmacological Target in Inflammatory Diseases and Cancer	Ribon Therapeutics	ERIBA Friday Seminar

INVITED SPEAKERS 2023.1

Date	Invited Speaker	Host	Title of the talk	Institute	Event
23/11/2023	Elly Tanaka	Eugene Berezikov	Triggering limb regeneration	Institute for Molecular Pathology, Vienna	Molecular Medicine Seminar Series
15/06/2023	Jason Sheltzer	Floris Foijer	Oncogene-like addiction to aneuploidy in human cancers	Yale School of Medicine	Molecular Medicine Seminar Series
13/01/2023	Rifka Vlijm	Ellen Nollen	Automated super resolution STED microscopy to study Archeal cell division	Rijks University, Groningen	Molecular Medicine Seminar Series
07/07/2023	Bart Eggen	Ellen Nollen		UMCG	Molecular Medicine Seminar Series
09/02/2023	Björn Schumacher	Marco Demaria	Genome instability in aging and disease	University of Cologne	Molecular Medicine Seminar Series
23/03/2023	Elsa Logarinho	Marco Demaria	Aging and Aneuploidy, i3S - Instituto	University of Porto	Molecular Medicine Seminar Series
06/04/2023	Sara Hägg	Marco Demaria	Causal inference studies of human biological aging – a geroscientific approach	Karolinska Institute, Stockholm	Molecular Medicine Seminar Series
25/05/2023	Morten Scheibye-Knudsen	Marco Demaria	Towards Interventions in Human Aging	University of Copenhagen	Molecular Medicine Seminar Series
07/12/2023	Benoit Palancade	Liesbeth Veenhoff	The nuclear pore complex: a safe place for gene expression	CNRS, Institut Jacques Monod	ERIBA Friday Seminar
24/04/2023	Manuel Müller	John LaCava	Probing Life and Death Decisions with Protein Semisynthesis	Kings College London	Molecular Medicine Seminar Series
02/05/2023	Waring “Buck” Trible	John LaCava	The molecular basis of caste development and evolution in ants		ERIBA Friday Seminar
20/07/2023	Victoria Belanchio	John LaCava	Unraveling the mysteries of LINE-1 retrotransposon expression	Tulane University School of Medicine	Molecular Medicine Seminar Series
17/10/2023	Rodoniki Athanasiadou	John LaCava	Complex Diseases: three stories from the lab about mechanisms and causal candidates	The Rockefeller University	ERIBA Friday Seminar
19/10/2023	Benjamin Greenbaum	John Lacava	The self/nonself discrimination problem in cancer evolution	Memorial Sloan Kettering Cancer Center	Molecular Medicine Seminar Series
10/03/2023	Barbara Bakker	Folkert Kuipers	Functional genetics of rare movement disorders	University Medical Center Groningen	ERIBA Friday Seminar
31/03/2023	Mihai G Netea	Folkert Kuipers	Variation and adaptation in immune responses	Nijmegen University	ERIBA Friday Seminar
14/04/2023	Dineke Verbeek	Folkert Kuipers	Functional genetics of rare movement disorders	University Medical Center Groningen	ERIBA Friday Seminar
02/06/2023	Stefan Willems	Folkert Kuipers		University Medical Center Groningen	ERIBA Friday Seminar
28/09/2023	Michael Hall	Groningen Jena Aging Meeting	mTOR signaling in growth and metabolism	Biozentrum, University of Basel, Switzerland	Groningen Jena Aging Meeting 2023
29/09/2023	Linda Partridge	Groningen Jena Aging Meeting	Ageing: a gut feeling	UCL, London, UK	Groningen Jena Aging Meeting 2023
30/09/2023	James (Jim) Kirkland	Groningen Jena Aging Meeting	Clinical studies of agents targeting aging mechanisms: the Translational Geroscience Network	Mayo Clinic, Rochester, USA	Groningen Jena Aging Meeting 2023

INVITED SPEAKERS 2023.2

Date	Invited Speaker	Host	Title of the talk	Institute	Event
29/09/2023	Vishwa Deep Dixit	Groningen Jena Aging Meeting	Metabolic control of inflammaging	Yale School of Medicine, New Haven, USA	Groningen Jena Aging Meeting 2023
29/09/2023	George Garinis	Groningen Jena Aging Meeting	DNA damage and innate immune responses during aging	University of Crete	Groningen Jena Aging Meeting 2023
29/09/2023	Malene Hansen	Groningen Jena Aging Meeting	Regulation of autophagy in aging and disease	The Buck Institute, Novato, USA	Groningen Jena Aging Meeting 2023
29/09/2023	Raffaella di Micco	Groningen Jena Aging Meeting	Exploiting senescence immunogenicity for leukemia treatment	I.R.C.C.S. Ospedale San Raffaele, Milano, Italy	Groningen Jena Aging Meeting 2023
29/09/2023	Alessandro Ori	Groningen Jena Aging Meeting	The aging brain proteome of a short-lived vertebrate	Genentech, South San Francisco, USA & Leibniz Institute on Aging - Fritz Lipmann Institute (FLI), Jena, Germany	Groningen Jena Aging Meeting 2023
29/09/2023	Björn Schumacher	Groningen Jena Aging Meeting	Genome Stability in aging and inheritance: new insights from C. elegans	CECAD, University of Cologne, Germany	Groningen Jena Aging Meeting 2023
29/09/2023	Maximina Yun	Groningen Jena Aging Meeting	Towards uncovering the basis of negligible senescence in vertebrates: enter the salamander	Center for Regenerative Therapies TU Dresden, Germany	Groningen Jena Aging Meeting 2023
28/09/2023	Milos Filipovic	Groningen Jena Aging Meeting	“Age-induced thiol oxidation predisposes brain for neurodegeneration via aberrant phase separation	Leibniz Institute for Analytical Sciences, ISAS, Berlin, Germany	Groningen Jena Aging Meeting 2023
28/09/2023	Janine Kirstein	Groningen Jena Aging Meeting	The role of chaperones in the phase-separation of Huntingtin	Leibniz Institute on Aging - Fritz Lipmann Institute (FLI), Jena	Groningen Jena Aging Meeting 2023
28/09/2023	Dudley Lamming	Groningen Jena Aging Meeting	When a calorie is not just a calorie: The regulation of health and longevity by dietary macronutrients	University of Wisconsin-Madison, USA	Groningen Jena Aging Meeting 2023
28/09/2023	Peter Tessarz	Groningen Jena Aging Meeting	Metabolism-epigenetics crosstalk in ageing	Max Planck Institute for Biology of Ageing, Cologne, Germany	Groningen Jena Aging Meeting 2023
28/09/2023	Sanne van der Rijt	Groningen Jena Aging Meeting	Targeting phospholipid metabolism via Pla2g15 results in reduced senescence in murine kidney and increases longevity in C. elegans	Amsterdam UMC, The Netherlands	Groningen Jena Aging Meeting 2023
28/09/2023	Friedrich Becker	Groningen Jena Aging Meeting	Dietary vitamin A restriction rescues declines in liver fat metabolism and ameliorates sarcopenia in aging mice	Leibniz Institute on Aging - Fritz Lipmann Institute (FLI), Jena	Groningen Jena Aging Meeting 2023
28/09/2023	Sasha Zhernakova	Groningen Jena Aging Meeting	Biological aging markers in population cohorts - microbiome and more	University Medical Center Groningen, The Netherlands	Groningen Jena Aging Meeting 2023
28/09/2023	Aki Minoda,	Groningen Jena Aging Meeting	Mu-kin Mouse Ageing Atlas: How the microbiota affect ageing	RIMLS, Radboud University Nijmegen, The Netherlands	Groningen Jena Aging Meeting 2023

INVITED SPEAKERS 2023.3

Date	Invited Speaker	Host	Title of the talk	Institute	Event
28/09/2023	Dennis De Bakker	Groningen Jena Aging Meeting	Microbiota transplantation can mitigate age-related brain inflammation and functional decline in a model of spontaneous Alzheimer’s-like pathology	Leibniz Institute on Aging - Fritz Lipmann Institute (FLI), Jena, Germany	Groningen Jena Aging Meeting 2023
29/09/2023	Raffaella di Micco	Groningen Jena Aging Meeting	Exploiting senescence immunogenicity for leukemia treatment	I.R.C.C.S. Ospedale San Raffaele, Milano, Italy	Groningen Jena Aging Meeting 2023
29/09/2023	Akiko Mammoto	Groningen Jena Aging Meeting	Endothelial senescence in hypoxia-induced lung vascular remodelling	Medical College of Wisconsin, USA	Groningen Jena Aging Meeting 2023
29/09/2023	Mihai Netea	Groningen Jena Aging Meeting	Impact of aging on trained immunity	Radboud MC, Nijmegen, the Netherlands/ Limes, University of Bonn, Germany	Groningen Jena Aging Meeting 2023
29/09/2023	Enric Urena Sala	Groningen Jena Aging Meeting	Exploring the mechanisms of action of the life-extending drug trametinib in Drosophila	University College London, UK	Groningen Jena Aging Meeting 2023
29/09/2023	Patrick Schädel	Groningen Jena Aging Meeting	Oxylipins as novel biomarkers of cellular and organismal inflammaging	Friedrich Schiller University, Jena, Germany	Groningen Jena Aging Meeting 2023
29/09/2023	Julia von Maltzahn	Groningen Jena Aging Meeting	Muscle stem cells in age and disease	B-TU Cottbus-Senftenberg, Germany	Groningen Jena Aging Meeting 2023
29/09/2023	Alberto Minetti	Groningen Jena Aging Meeting	Proteostasis stress delays regeneration following injury in old small intestine epithelium	Leibniz Institute on Aging - Fritz Lipmann Institute (FLI), Jena, Germany	Groningen Jena Aging Meeting 2023
29/09/2023	Hugo Fernandes	Groningen Jena Aging Meeting	Unlocking the regenerative potential of extracellular vesicles: Bioactivity enhancement through miRNA modulation	University of Coimbra, Portugal	Groningen Jena Aging Meeting 2023
29/09/2023	George Garinis	Groningen Jena Aging Meeting	DNA damage and innate immune responses during aging	University of Crete, Greece	Groningen Jena Aging Meeting 2023
29/09/2023	Björn Schumacher	Groningen Jena Aging Meeting	Genome Stability in aging and inheritance: new insights from C. elegans	CECAD, University of Cologne, Germany	Groningen Jena Aging Meeting 2023
29/09/2023	Rouven Arnold	Groningen Jena Aging Meeting	Unravelling protective mechanisms of aging: A new role for histone chaperone HIRA	SBP Medical Discovery Institute, La Jolla, USA	Groningen Jena Aging Meeting 2023
29/09/2023	Mihailo Mirkovic	Groningen Jena Aging Meeting	Introns drive asymmetric chromosome inheritance in ageing	ETH, Zürich, Switzerland	Groningen Jena Aging Meeting 2023
30/09/2023	Thomas Bosch	Groningen Jena Aging Meeting	Longevity, cellular senescence and the microbiome - lessons from the non-senescent model Hydra	Christian Albrechts University of Kiel, Germany	Groningen Jena Aging Meeting 2023
30/09/2023	Johannes Krug	Groningen Jena Aging Meeting	The transparent klara line as a tool for in vivo analyses	Leibniz Institute on Aging - Fritz Lipmann Institute (FLI), Jena, Germany	Groningen Jena Aging Meeting 2023
30/09/2023	Jochen Mierau	Groningen Jena Aging Meeting	Socioeconomic aspects of health and lifespan extension therapies	Lifelines, University of Groningen, The Netherlands	Groningen Jena Aging Meeting 2023

FACILITIES

FUNCTIONAL GENOMICS CENTRE IPSC/CRISPR FACILITY
SEQUENCING FACILITY

FUNCTIONAL GENOMICS CENTRE IPSC/CRISPR FACILITY

The discovery of protocols to reprogram somatic cells into induced pluripotent stem cells (iPSCs) is revolutionizing 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. In addition, we facilitate genome-wide CRISPR functional screens and together with the Netherlands Cancer Institute and Leiden University we form a national KWF-funded CRISPR screen infrastructure – ScreeninC - supporting CRISPR screens at the national level. Our role in this consortium is to develop CRISPR-screens in complex model systems such as organoids (in collaboration with Jarno Drost at the Princess Maxima Centre), in iPSCs, and in mice (in collaboration with Bart van de Sluis, UMCG)

Since the start of the center in 2016, we accommodated >130 different projects for more than 60 different groups. As part of these projects, we implemented a number of differentiation protocols and protocols to grow cerebral organoids. In addition to supporting ‘standard’ CRISPR KO services, we also implemented protocols to genome-engineer tags onto genomic loci and introduce point mutations of choice into various cell lines, including iPSCs. So far, we supported/are supporting more than 10 CRISPR screens since the start of the KWF-funded ScreeninC consortium. While we support all types of CRISPR screens (including CRISPRa and CRISPRi), our current development goals are to implement and validate ‘complex’ CRISP screens such as screens in iPSCs, organoids or in mice. For the latter, we are, together with Bart van der Sluis, developing a somatic CRISPR screen in liver to identify modulators of liver cancer. We therefore expect that support of CRISPR screens will become an important task for our team in the coming years.

Importantly, we regularly host MSc students for internships and we each year we organize the CRISPR genome engineering course for Biomedical Sciences MSc students, the JSM course ‘Model systems in ageing research’ for third year medical students and host medical students for the BSc theses. Importantly, we trained many PhD students and postdocs in deriving and maintaining iPSCs and in differentiating iPSCs into various cell types.

WHO

Floris Foijer Coordinator Functional Genomics Centre
Mathilde Broekhuis Lab manager
Petra L. Bakker Project manager
Marilucrezia Losito Postdoctoral fellow
Laura Kempe Research technician
René Wardenaar Bioinformatician

CONTACT

European Research Institute for the Biology of Ageing
University Medical Centre Groningen

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Internal Zip Code FA50
9700AD Groningen

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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 copy-number neutral structural genomic aberrations such at inversions and translocations in individual cells. As Strand-seq requires one passage of culture, we also developed a simplified version of this protocol - shallow single cell whole genome sequencing (scsWGS) – for which cells do not need to be cultured. While this technique cannot detect balanced translocations, inversions, or sister chromatid exchange events, it is a very powerful tool to quantify copy number changes as small as 250 kb in single cells without the need of culturing the cells. Over the past few years, we accommodated ~30 scsWGS projects for ~20 PIs each year.

In addition to offering our single cell DNA services to customers, we are also developing new applications of these protocols such as single cell ATAC-seq, single cell-exome-seq, and single-cell CRISPR. Finally, we are testing a lower cost pipeline for scsWGS, which we hope to implement in 2024 and which we expect will help the facility to grown further.

In addition to our single cell DNA services (Strand-seq and scsWGS), we also support single cell and bulk RNA sequencing. In addition to various commercial kit-based bulk RNA sequencing library protocols (inquire for more information), we also implemented RNA-seq protocols based on SMART3-seq chemistry. As the latter library preparation protocols were developed in house, these protocols are much more cost friendly, and we expect that our SMART3-seq services will grow substantially in the coming years.

For single cell RNA sequencing, we have mostly made use of the commercial 10X Genomics platform. At the end of 2023, we purchased a lower cost alternative of this platform (Seekgene), which we are currently implementing and through which we expect that demand for scRNA-seq will grow. In addition to implementing a Seekgene pipeline, we are also developing our own SMART3-seq-based scRNA pipline, which we hope to implement in 2024.

Finally, in 2023, we started preparing on a plan to merge the Research Sequencing Facility and Functional Genomics Center into a newly established private company that will commercialize the services of both facilities to help both facilities to become self-sustainable in the coming years. For more details, see chapter ‘Functional Genomics Center’.

WHO

Diana Spierings Coordinator Research Sequencing Facility
Nancy Halsema Technician
Rianna Arjaans Technician
Jennefer Beenen Technician
Erik Hiddingh 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 Medicine and Innovative Treatment

MODEL ORGANISMS WEEK. PART OF MMIT* EXPERIMENTAL TECHNIQUES IN RESEARCH COURSE

25-28 students 9 ECTS

Coordinators **Michael Chang** and **Liesbeth Veenhoff**

Objective

The course 'Experimental techniques in research' provides an overview of good research practices (statistics, graphing, R-programming) and state-of-the-art techniques in several areas of biomedicaland pharmaceutical research, including genomics, animal models, imaging, protein research, and translational research. This 6-week course will provide an overview of basic research-related skills (statistics, graphing, Rprogramming) and state-of-the-art techniques in several areas of biomedical- and pharmaceutical research, including genomics, animal models, imaging, protein research, and translational research. Established researchers will introduce these skills and techniques and present their current research to demonstrate how these skills/techniques can be used to answer a specific research question.In the first week basic research skills in statistics, R-programming, and graphing will be taught and this week will not be graded. In the following 5 weeks, you will work on week-related topics, which will finish on Friday with a presentation or other type of evaluation.

MOLECULAR BIOLOGY OF AGEING AND AGE-RELATED DISEASES

20 students; 5 ECTS

Co-Coordinator **Michael Chang**

Objective

Ageing can be defined as the gradual loss of the ability of the organism to maintain homeostasis. 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 will evaluate to what extent the up-to date knowledge on the molecular biology provides opportunities for interventions, also when considering what we learn from evolutionary theories of ageing. 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.

TRACK ON BIOLOGY OF HEALTHY AGEING AND DISEASE (PROGRAMME)

MSc CRISPR Course

30 students 5 ECTS

Co-coordinator **Floris Foijer**

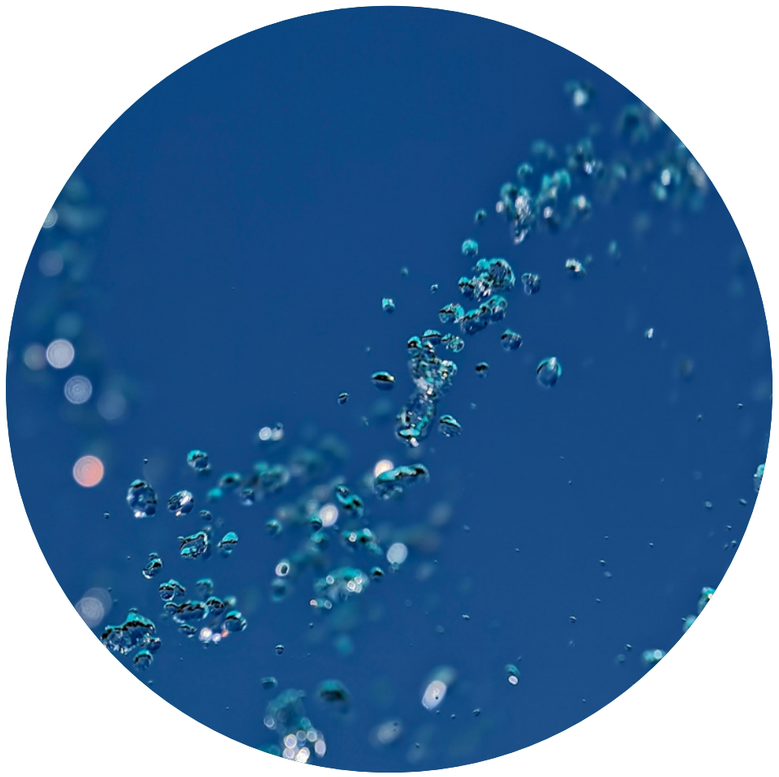
Objectives
In this course, MSc learn the basics of CRISPR engineering. Students learn about the history and various applications of CRISPR including knockouts, knockins,CRISPR I, CRISPRa, mutations and genome-wide screens. Furthermore, they get hands-on experience in the designof guide RNAs and genome 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.

MODEL ORGANISMS IN AGEING RESEARCH COURSE

14 students 3 ECTS (JSM BSc course)

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.

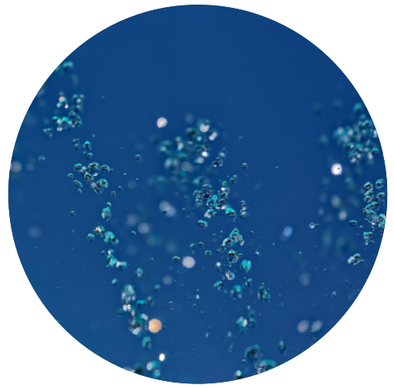


RESEARCH PROJECT BIOMEDICAL SCIENCES – AGEING RESEARCH ERIBA

12 students 10 ECTS

Coordinator **Cor Calkhoven**

Objective
Bachelor's Research Projects are provided by and embedded within a research group, and supervised by experts in the field. Based on the topic category, projects are grouped in clusters. Students choose a Bachelor's Research Project from an overview of possible topics ('project pool') within the major. Project pool is gathered and published by a major-specific course coordinator. Two students are matched with a project of their preference and introduced to their project partner and project supervisor(s). Supervisors provide students with an introduction to the project and a start-up literature. Based on that information, students are given a few days to develop their project plan. This entails individual work on drafting an introduction to the project and a research proposal. The proposals are discussed together with the supervisor and a final version of a project plan is designed. The students execute the experiments as a team to collect and analyze the data. Experiments are executed in either laboratories, field, and/or online. Students also participate in research group activities with their supervisors (e.g. research meetings, progress meetings, journal clubs) and exchange their knowledge by interacting with their peers, supervisors and scientists within their research project environment. Students' research outcomes are disseminated during the final presentation session and the conclusions are discussed with fellow students and the associated supervisors. Each student writes a scientific report on the Bachelor's Research Project, in which the 'materials and methods'; as well as the 'results'; (to an extent) can be shared between the two team members, whereas the 'introduction'; and 'discussion'; are individually composed. Reports are to be handed in on the last day of the course.

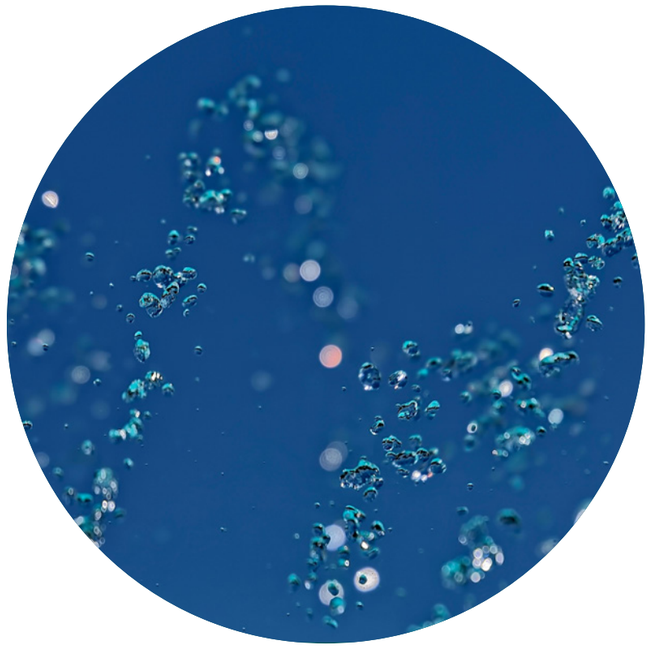


CURRENT THEMES IN HEALTHY AGEING

Masters, 5 ECTS

Coordinator **Marco Demaria, Michael Chang** (instructor)

Objective
This course will teach students how to prepare for attendance of scientific seminars given by eminent researchers, how to extract all relevant information from seminars and how to place the presented scientific content into the context of the field. The course will start with an introduction lecture, explaining the learning goals and practicalities of this course. This introductory lecture will be followed by two lectures that cover basic and translational aspects of aging. At the beginning of the course, you select 6 seminars from the weekly UMCG Molecular Medicine seminars series or, depending on availability, online seminars selected by the course coordinators. You will get the opportunity to participate actively and meet the speaker following the seminar. Prior to the seminars, you will prepare the seminar by literature study and writing a preparatory report. For four of the seminars you attended, you will write a full report. You will be actively involved in peer and self- assessment of the full reports. During the first semester, you will select the topic of 1 of the attended seminars and select additional papers and reviews to expand your knowledge on the topic, and to identify and develop possible follow-up questions. Afterwards, in semester 2A, you will prepare a presentation on this topic and discuss your topic and favored follow-up project with your peers and the coordinators. This presentation should cover an overview of the additional literature and the state-of-the art, and your perspectives on the field. A lecture on how to prepare this presentation will be given at the end of the first semester by one of the coordinators. There will be 2 fixed dates for these end presentations. During the session, you are expected to actively participate in the discussion, and to contribute to peer assessment. At the end of the course, you will write a brief essay on your learning process in this course.



ERIBA AGEING COURSE
8 PhD students 1 ECTS

Coordinator **Marco Demaria**

Objective
The ERIBA organizes a course for all our first-year PhD students. The course consists in 1 lecture/month where an ERIBA PI will talk about her/his research and perspectives in the field.The course is highly interactive, and discussion is mandatory. In addition to first-year students, we highly encourage ALL the students that did not participate a previous edition of the course to do so.

Oncology Track **(MMIT* course)**
Coordinator: **Marco Demaria**

DATA SCIENCE IN BIOMEDICINE
100 students 5ECTS

Coordinator **Victor Guryev**

Objective
Biomedical sciences is a fast evolving multidisciplinary research knowledge field in which new disciplines, like bioinformatics, have advanced rapidly during recent years. This course offers students an introduction into: computational biology, programming andbig-data management. Students will be trained to: mine for genetic diseases in international databases, analyze and visualize transcriptome data, read and edit programs written in R and Python and visualize data in R and Python. This course prepares the master students for the FSE/FMW learning line “Datascience”.

TOPCLASS II: MODEL ORGANISMS WEEK (PART OF MMIT* EXPERIMENTAL TECHNIQUES IN RESEARCH COURSE)
25-28 students 9 ECTS

Coordinators **Liesbeth Veenhoff** and **Michael Chang**

Objective
The course ‘Experimental techniques in research’ provides an overview of good research practices (statistics, graphing, R-programming) and state-of-the-art techniques in several areas of biomedicaland pharmaceutical research, including genomics, animal models, imaging, protein research, and translational research. This 6-week course will provide an overview of basic research-related skills (statistics, graphing, Rprogramming) and state-of-the-art techniques in several areas of biomedical- and pharmaceutical research, including genomics, animal models, imaging, protein research, and translational research. Established researchers will introduce these skills and techniques and present their current research to demonstrate how these skills/techniques can be used to answer a specific research question.In the first week basic research skills in statistics, R-programming, and graphing will be taught and this week will not be graded. In the following 5 weeks, you will work on week-related topics, which will finish on Friday with a presentation or other type of evaluation.

MOLECULAR BIOLOGY OF AGEING AND AGE-RELATED DISEASES MSC BMS
25 Master students 5 ECTS

Coordinator **Liesbeth Veenhoff**

Objective
Ageing can be defined as the gradual loss of the ability of the organism to maintain homeostasis. 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 will evaluate to what extent the up-to date knowledge on the molecular biology provides opportunities for interventions, also when considering what we learn from evolutionary theories of ageing. 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.

PROTEINS AND PROTEOME (MMIT* COURSE)
20 students
Current Themes in Healthy Ageing

Co-Coordinators **Judith Paridaen and Marco Demaria, Michael Chang** (instructor)

Objective

This course will teach students how to prepare for attendance of scientific seminars given by eminent researchers, how to extract all relevant information from seminars and how to place the presented scientific content into the context of the field. The course will start with an introduction lecture, explaining the learning goals and practicalities of this course. This introductory lecture will be followed by two lectures that cover basic and translational aspects of aging. At the beginning of the course, you select 6 seminars from the weekly UMCG Molecular Medicine seminars series or, depending on availability, online seminars selected by the course coordinators. You will get the opportunity to participate actively and meet the speaker following the seminar. Prior to the seminars, you will prepare the seminar by literature study and writing a preparatory report. For four of the seminars you attended, you will write a full report. You will be actively involved in peer and self- assessment of the full reports. During the first semester, you will select the topic of 1 of the attended seminars and select additional papers and reviews to expand your knowledge on the topic, and to identify and develop possible follow-up questions. Afterwards, in semester 2A, you will prepare a presentation on this topic and discuss your topic and favoured follow-up project with your peers and the coordinators. This presentation should cover an overview of the additional literature and the state-of-the art, and your perspectives on the field. A lecture on how to prepare this presentation will be given at the end of the first semester by one of the coordinators. There will be 2 fixed dates for these end presentations. During the session, you are expected to actively participate in the discussion, and to contribute to peer assessment. At the end of the course, you will write a brief essay on your learning process in this course.

PUBLIC OUTREACH & DISSEMINATION

EVENTS OUTREACH COMMITTEE ACTIVITIES

Committee members in the image

Anne de Groot – PhD-student
Eric Hiddingh – Technician
Clément Karch – PhD-student
Laura Kempe – Technician
Natalia Skinder – PhD-student
Mattia Stranges – PhD-student
Andrea Tijhuis – PhD-student

ERIBA PhD Committee

The ERIBA Phd committee is a group of ERIBA employees (technicians, PhD-students, and post-docs) that organize social events for the whole institute. The main goal of the committee is to offer opportunities in which employees from different research groups, facilities, and management teams can get to know each other, exchange research ideas, and have fun together.

Within ERIBA there are weekly seminars where PhD-students, post-docs and external speakers can present their research. We organize weekly “Borrels” in which it is possible to chat with the speakers of the ERIBA seminar. In addition, we organize a monthly borrel with each month a different activity. As there a many different nationalities working in ERIBA, we highlight different cultures during these monthly activities. Some recent examples are the German-themed Oktoberfest “Borrel” and the Dia de los Muertos celebration during the Mexican-themed “Borrel”. In addition to the “Borrels”, we also organize extra activities, such as movie nights in the Marten Hofkerzaal and opportunities to have dinner together. Yearly, together with the ERIBA secretary, we organize a New Year toast and a Christmas potluck dinner. A highlight of 2023 was ERIBA’s 10th year anniversary celebration. We organized multiple activities so that ERIBA employees and alumni, could celebrate the 10th year anniversary together.

EVENTS

Scientific conferences/meetings organised by ERIBA in 2022 and 2023 include

7th INTERNATIONAL CELL SENESCENCE ASSOCIATION (ICSA) CONFERENCE- 29 Sep- 1 Oct 2022

Scientific organisers
Marco Demaria (ERIBA, UMCG), Andrea Maier, Peter de Keizer (UMC, Utrecht)

The Programme of the conference consisted of seven sessions covering exciting topics related to the Senescence. For each session, two leading scientists introduced the topic and presented their latest work. Additionally, speakers selected from submitted abstracts shared their research in each session.

The meeting was an outstanding platform where established as well as young scientists presented their work and actively participated in the meeting. The keynote lectures by distinguished scientists like Judith Campisi (Buck Institute, USA), Valery Krizhanovsky, Weizmann Institute of Science, Israel and Pura Munoz-Canoves, Universitat Pompeu Fabra, Spain inspired the attendees and motivated the young scientists.

GRONINGEN JENA AGEING MEETING (G-JAM) 2023 – 28-30 September 2023

Scientific Organisers
Cor Calkhoven (ERIBA, UMCG), Ellen Nollen(ERIBA, UMCG), Eugene Berezikov (ERIBA, UMCG), Caludia Waskow (FLI, Jena, Germany), Bjorn von Eyss (FLI, Jena, Germany)and Helen Morrison (FLI, Jena, Germany).

The Groningen Jena Aging Meeting (G-JAM) 2023 was held at the European Research Institute for the Biology of Ageing (ERIBA), 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.

The keynote lectures by distinguished scientists like Michael Hall, Biozentrum, University of Basel, Switzerland, Linda Partridge, UCL, London, UK, James (Jim) Kirkland, Mayo Clinic, Rochester, USA encouraged the scientists.

DUSRA ANNUAL MEETING 15-16 June 2023

Scientiific organizers
Eline Slagboom (Leiden University), Ellen Nollen (ERIBA, University Medical Center Groningen), Joris Hoeks (Maastricht University), Peter de Keizer (University Medical Center Utrecht) and Pol Grootwagers (Wageningen University).

OUTREACH COMMITTEE

Various Outreach activities are organised by the ERIBA outreach commitee

Members of the Outreach Committee
Judith Paridaen
Anton Steen
Maria Suarez
Soraya Wobben
Annemiek Veldsink
Stijn Mouton
Suzanne Couzijn
Lotte Steeneken
Andréa Tijhuis
Megha Pandey
Läle Güngördü
Josephine Hartung
Katya Dvorinova
Karin van Wageningen

ACTIVITIES 2022

JONGE ONDERZOEKERS
17-05-2022

Staff member involved: **Stijn Mouton**

10 children aged 8-12 years via Jonge Onderzoekers institute visited ERIBA for a tour at the lab. Stijn introduced some lab work to them. They did activities with microscope and pipettes.

Groningen - De Jonge Onderzoekers Groningen & Eemsdelta
djog.nl

ZPANNEND ZERNIKE
01-10-2022

Staff member involved: **Anton Steen**

Like every year ~800 visitors. Outreach; DNA from a banana, Microscope, stickers, escape room. Co-organizer Anton Steen ERIBA Outreach committee member

Home - Zpannend Zernike
zpannendzernike.nl

FRANEKER EXPEDITIE NEXT AT FRANEKER
06-05-2022

This was an event organized in Franeker (Friesland) especially to introduce the biomedical lab work to children. ERIBA had a stand with the activities like withdraw DNA from a banana, Escape room and stickers. 250 children aged between 10-12 years attended the event.

Expeditie NEXT | Academie van Franeker
academiefraneker.nl

SCHOOL UIT WASKEMEER
21-12-2022

20 VWO students visited ERIBA and took a tour of the labs.

www.csgliudger.nl/ontdek-onze-school/waskemeer/

ACTIVITIES 2023

STUDENT VAN SCHOLIERENACADEMIE
September 2022 - July 2023

Developing project for training package for secondary education on Healthy Ageing

Scholierenacademie | Maatschappij/bedrijven | Rijksuniversiteit Groningen
www.rug.nl/society-business/scholierenacademie/

OPEN DAY UMCG
10-06-2023

Staff involved: **Anton Steen, Emma Dijkstra and Amarins Blaauwbroek**

~1200 visitors; Microscope looking at fishes

Terugblik open dag - umcg.nl
www.umcg.nl/opendag

RESEARCHERS' NIGHT AT THE FORUM GRONINGEN.
29-09-2023

Involved staff: **Anton Steen, Tegan Otto** and **Soraya Wobben**

The researchers' night was organized the Groningen Forum. ERIBA scientists opted the 'Pipeteren, kun je leren' theme. This is a Europe-wide public event, which showcases the diversity of science and its impact on citizens' daily lives in fun, inspiring way.The European Researchers' Night is co-funded by the European Commission, under the Marie Skłodowska-Curie Actions.

European Researchers Night
forum.nl

ZPANNEND ZERNIKE
30-9-2023

Involved staff: **Anton Steen** and **ERIBA Outreach committee members**

~840 visitors attended the event at the UMCG. Various activities were organised by the outreach committee.

Home - Zpannend Zernike
zpannendzernike.nl

SOCIAL MEDIA
Lale Güngördü and **Josephine Hartung** started a very successful ERIBA social media account on Instagram. ~35 posts on Facebook and Instagram were made last year. Now Maria Suarez is handling the account.

MEDIA
14-12-2023

On December 14th RTV NOORD paid attention to ERIBA's 10th anniversary. **Ellen Nollen** was in the studio to talk about the research being done in ERIBA. Cor Calkhoven also contributed to the talk show. The show was hosted by Eva Hulscher (RTV Noord presenter)

Verouderingsonderzoek Eriba bestaat 10 jaar: **Zoeken naar medicijnen om gezond te blijven** - RTV Noord

SCIENTIFIC ADVISORY BOARD

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Developmental Biology

Chair of the Department of
Anatomy and Embryology
Leiden University Medical Center

The Netherlands

Helle Ulrich
Executive Director of the
Institute of Molecular Biology

Professor at the Faculty of Biology
University of Mainz

Germany

Johan Auwerx
Professor and
Nestle Chair
in Energy Metabolism

Ecole Polytechnique Federale
in Lausanne

Switzerland

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Associate Professor
of Biochemistry

Department of Biology
ETH Zurich

Switzerland

SPONSORS

ERIBA

The European Research Institute
for the Biology of Ageing
was made possible
thanks to the support of

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Ministerie van Economische Zaken

The Province of Groningen

provincie groningen

Collaboration of the Northern
Netherlands (SNN)

SNN

The European Union

European Union
European Regional Development Fund

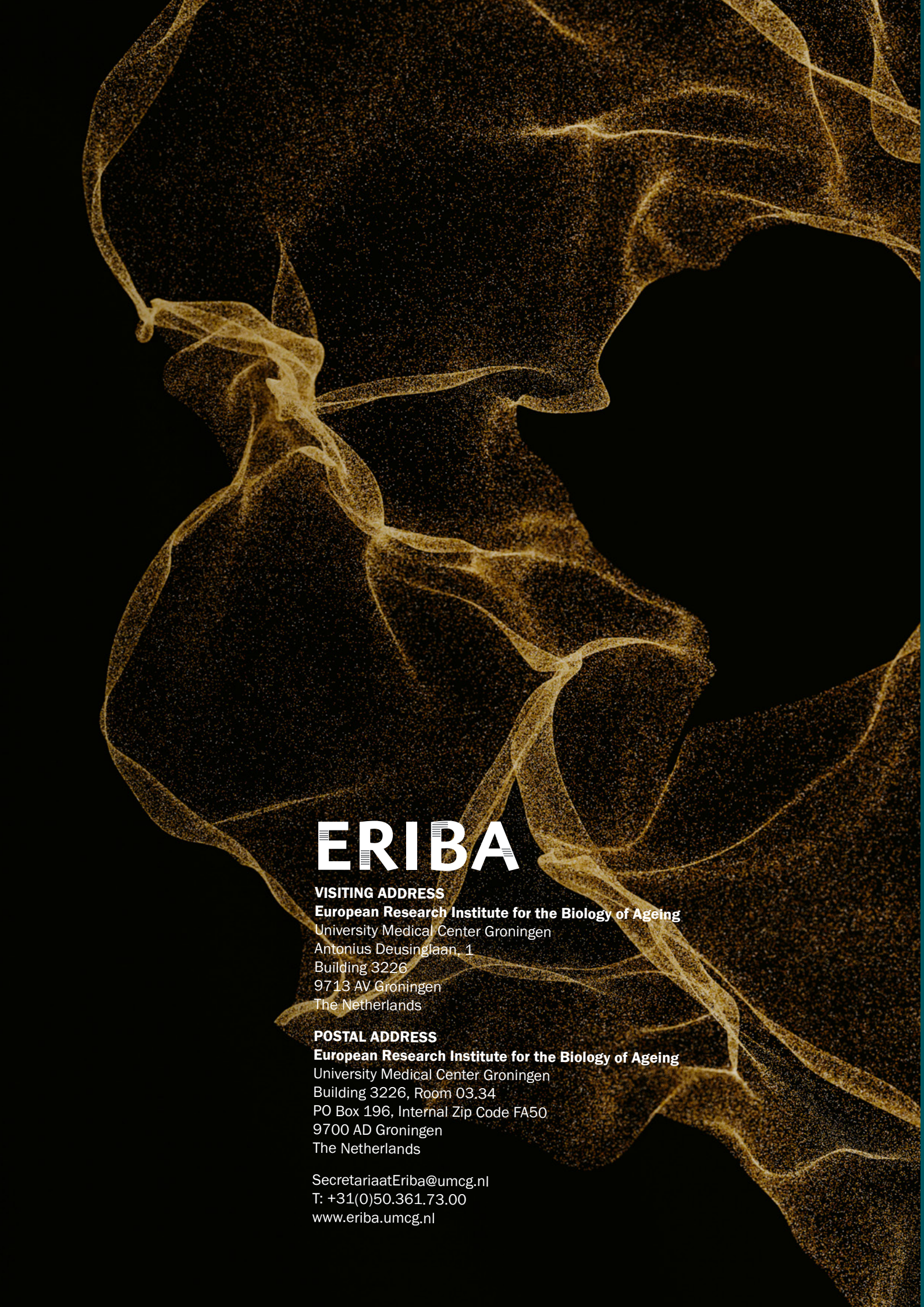
Investing in your future!

The Noaber Foundation

noaber foundation

The Pediatric Oncology
Foundation Groningen (SKOG)

SKOG
stichting kinderoncologie groningen



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