CALL FOR TWO RESEARCH FELLOWSHIPS (BI)

Fellowship References GIMM/BI/34a-2025 and GIMM/BI/34b-2025

Gulbenkian Institute for Molecular Medicine (GIMM) opens a call for 2 (two) Research Fellowships designated **"NOS Alive – GIMM 2025 Research Fellowship"**, within the scope of the partnership established between the GIMM Foundation – Gulbenkian Institute for Molecular Medicine (GIMM) and Everything is New, the promoter of the NOS Alive. For this call, the GIMM Foundation is offering four research projects in different scientific areas. The two selected candidates will have the opportunity to choose which project they wish to develop. These fellowships are funded by Everything is New, under the following conditions:

Scientific Area(s): Biology and Life and Health Sciences

Fellowship recipients / Admission requirements*:* Any National, foreign and stateless candidate(s) that fulfill the necessary conditions to be enrolled in a non-academic degree course (in area related to the work plan) can apply. Are considered "Non-academic degree courses" the ones referred in paragraph e) of number 3 of article 4 of Decree-Law nr 74/2006, from 24th March, in its current version, as long as they are developed in association and cooperation between a higher education institution and at least one R&D Unit in accordance with the provisions of paragraph e) of Article 3 of FCT Fellowship Regulation.

Applicants must hold the following requirements:

- Holder of a Bachelor's and/or Master's degree in Biology or a related field (mandatory requirement), with the most recent degree completed after January 2021;
- Excellent command of spoken and written English.

Work Plan and Objectives:

- Project 1: "How inflammatory cytokines rewire cardiac RNA splicing in aging" (Annex 1);
- Project 2: "Mechanistic Links between RNA Splicing Deterioration and Cellular Senescence" (Annex 1);
- Project 3: "Targeting immune-stem cell interactions in aging to restore organ health" (Annex 1);
- Project 4: "AGEWISE: Unravelling the Gut-Hormone Axis in Women's Ageing" (Annex 1).

Legislation and Applicable Regulation: Estatuto do Bolseiro de Investigação (Lei n.º 40/2004, de 18 de Agosto, republished in attachment to Decreto-Lei n.º 202/2012, de 27 de Agosto, changed by ***Decretos-Leis n.º 123/2019, 28 de Agosto e nº 65/2024, 1 de outubro***) and current Regulation of Fellowships of GIMM.

Predicted start date, duration and renewal conditions: The fellowship contract is predicted to start in January 2026, for a period of 12 (twelve) months on an exclusive basis, non-renewable.

Work place and Scientific orientation: The research work will be carried out in one of the following laboratories at GIMM, with the possibility of conducting part of the work (maximum of two months) in a laboratory abroad:

- Project 1: Maria Carmo-Fonseca, RNA & Gene Regulation (https://gimm.pt/lab/maria-carmo-fonseca-lab/);
- Project 2: Joel Perez-Perri, RNA Regulation and Aging (https://gimm.pt/lab/joel-perez-perri-lab/);
- Project 3: Neves & Sousa-Victor, Aging & Tissue Repair (https://gimm.pt/lab/neves-sousa-victor-lab/);
- Project 4: Ana Santos Almeida, Microbiome in Health & Disease Translational Laboratory (https://care.gimm.pt/lab/microbiome-in-health-disease-translational-laboratory/).

Non-discrimination and equal access policy: GIMM undertakes to ensure compliance with the principles of non-discrimination and equality and to that extent, provides that no candidate can be privileged, benefited, harmed or deprived of any right or exempted from any duty due in particular ancestry, age, gender, sexual orientation, marital status, family status, economic status, education, social origin or condition, genetic heritage, reduced working capacity, disability, chronic disease, nationality, ethnic origin or race, place of origin, language, religion, political or ideological convictions and trade union membership.

International environment and experience: Diversity is a fundamental aspect of the essence of GIMM, where researchers and non-researchers of different nationalities, backgrounds and areas of study work together, promoting the exchange of experiences and interactions, contributing to the personal and professional development of each person and to the existence of an international, inclusive and stimulating environment.

Research Fellows Support Centre: The Research Fellows Support Centre works everyday from 09:00AM to 11:00AM at People & Culture Unit Office.

Fellowship financial conditions: The fellow will benefit from a monthly stipend in the amount of 1.309,64€ while in Portugal and 2.118,65€ while abroad, in accordance with the applicable regulations. The amount will be paid by wire transfer at the end of each month. The fellow will also benefit from a personal accident insurance to execute the proposed research activities as well as the right to Social Security through Voluntary Social Insurance regimen, if wanted, under the terms of Código dos Regimes Contributivos do Sistema Previdencial de Segurança Social, and the contributions costs will be supported by the research project.

Application documents: - Motivation Letter; - Detailed CV; - BSc and/or MSc certificate; - Contact of 1 reference; - Candidate's declaration of honor indicating previous fellowships, if any, its typology and duration.
The non-compliance with these requirements determines the immediate rejection of the application.
In case the applicant does not have yet the required degree certificate, a declaration of honor stating the conclusion of the necessary qualifications for the purposes of this process will be accepted and must be sent by the end date of the call.

Jury evaluation and selection: The applications will be evaluated by a selection panel composed of the following members:
- Maria Carmo-Fonseca, Group Leader, Gulbenkian Institute of Molecular Medicine (FMUL,GIMM)
- Joel Perez-Perri, Group Leader, Gulbenkian Institute of Molecular Medicine (GIMM)
- Joana Neves, Group Leader, Gulbenkian Institute of Molecular Medicine (GIMM)
- Pedro Sousa-Victor, Group Leader, Gulbenkian Institute of Molecular Medicine (GIMM)
- Ana Santos Almeida, Group Leader, Gulbenkian Institute of Molecular Medicine (GIMM)

Selection methods: The evaluation of applications and respective selection will be based on the following methods

1) **Document Evaluation (50%)** – In this phase, the candidates' Curriculum Vitae and motivation letter will be assessed on a scale from 0 to 10. Only candidates who score above 7 in this phase will be invited for an interview.
2) **Interview (50%)** – The selected candidates for this phase will be evaluated, also on a scale from 0 to 10.

The final score will result from the weighted average of the two phases (document evaluation and interview), each accounting for 50% of the total. The 2 (two) highest-ranked candidates will subsequently be invited to choose the research project they wish to develop, in order of ranking.

Deadlines and application process: The period to submit applicants starts on 10/07/2025 and ends on 10/09/2025. Applications must include all documents identified in ***"Application documents"*** section in a sole PDF document titled "*CandidateName*_BolsaNOSAlive2025.pdf". Alternatively, the reference letter may be sent directly by the referee(s). Applications should be submitted to the GIMM People & Culture Unit via email at positions@gimm.pt. The email subject line must include the reference "BolsaNOSAlive2025"_**GIMM/BI/34a-2025 and GIMM/BI/34b-2025.** ***The non-compliance with these requirements determines the immediate rejection of the application.***

Notification of results: Within 90 days after the termination of the applications submission deadline, both admitted and excluded candidates list and final classification list shall be communicated to all admitted candidates through email.

Preliminary Hearing and Final Decision Deadline: After notification, all candidates have 10 working days to respond. Panel's final decisions are pronounced within a period of 90 days, from application deadline.

Fellowship contracting: The Fellowship is granted through the signature of a contract between GIMM and the selected fellow and after the fellow send the following mandatory documents: copy of identification document (in case of non-European citizens is mandatory the work visa / valid resident permit), document proving the required academic degree and the document proving the enrollment in a non-academic degree course.
For each Fellowship period an Activity Report must be prepared by the fellow as well as the Report by the supervisor.

Lisbon and Oeiras, 9th of July 2025

The Executive Committee of GIMM
Professor Maria Manuel Dias da Mota

NOS Alive – GIMM 2025 Scholarships

Project #1

Title:

How inflammatory cytokines rewire cardiac RNA splicing in aging

Description:

The heart, like all organs, undergoes an aging process characterized by deterioration and increased vulnerability to disease, particularly heart failure. Chronic low-grade inflammation is a hallmark of aging and a shared target of longevity-promoting interventions. Cardiomyocytes express receptors for key pro-inflammatory cytokines—TNF, IL-1, and IL-6—which modulate the expression of genes that encode ion channels, gap junction proteins, and calcium-handling proteins such as ryanodine receptors. Importantly, cardiac aging is also associated with widespread alterations in RNA splicing, yet the upstream triggers of these changes remain unclear. We hypothesize that chronic exposure to low levels of pro-inflammatory cytokines directly alters RNA splicing patterns in cardiomyocytes, contributing to the functional decline observed in the aging heart. Main Objectives: 1) To determine the impact of chronic exposure to TNF, IL-1, and IL-6 on alternative splicing in human cardiomyocytes. 2) To identify splicing events in cytokine-treated cardiomyocytes that overlap with those observed in aging human and murine hearts. 3) To uncover molecular pathways linking inflammation-induced splicing changes to cardiac dysfunction. Methodology: We will use human induced pluripotent stem cell-derived cardiomyocytes (hiPSC-CMs) and treat them chronically with TNF, IL-1, and IL-6, mimicking an inflammatory aging environment. RNA will be collected at multiple time points and subjected to deep RNA sequencing. Differential splicing analysis will be performed using established computational pipelines. Splicing changes will be compared with publicly available transcriptomic datasets from aged human and mouse hearts to identify shared patterns and conserved mechanisms.

Lay Summary / Impact of the Study:

As we age, our hearts, like the rest of our bodies, become more vulnerable to disease. One key factor driving this process is chronic, low-level inflammation. Our project explores how inflammation affects heart cells at a very fundamental level—by altering how genes are read and processed. We will study how specific inflammatory molecules, called cytokines, influence in human heart cells grown in the lab. In particular, we are looking at how these molecules change the way genetic instructions are "spliced"—a process that shapes which proteins the cells produce. Changes in splicing have been linked to aging and heart disease, but we don’t yet understand what causes them. By uncovering how inflammation alters RNA

splicing in heart cells, our research could pave the way for new treatments that keep the heart healthier for longer.

Host lab at GIMM:

Maria Carmo-Fonseca, RNA & Gene Regulation (https://gimm.pt/lab/maria-carmo-fonseca-lab/)

External Collaboration:

Dr. Leslie Leinwand, University of Boulder Colorado, USA

Expected duration of the external collaboration:

1 month

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Project #2

Title:

Mechanistic Links between RNA Splicing Deterioration and Cellular Senescence

Description:

The accumulation of senescent cells is a hallmark of ageing. These cells exhibit irreversible growth arrest and secrete significant amounts of pro-inflammatory factors, which exert both local and systemic effects. Splicing occurs during messenger RNA (mRNA) biosynthesis and involves the removal of introns from precursor mRNA, generating a mature transcript that can be translated into a functional protein. Proper regulation and quality control of splicing are crucial for maintaining cellular function. Aberrantly spliced mRNAs can encode toxic proteins—either truncated or prone to aggregation—and are therefore rapidly degraded by cellular quality control mechanisms such as the exosome and the nonsense-mediated mRNA decay (NMD) pathway. Analyses of senescent cells have consistently revealed a widespread accumulation of splicing defects in the transcriptome. Furthermore, reduced activity of the splicing machinery alone is sufficient to induce senescence. While this clearly establishes a link between splicing defects and cellular senescence, the underlying mechanisms remain poorly understood. We hypothesize that the accumulation of aberrantly spliced RNAs triggers cellular senescence by sequestering RNA quality control or processing factors, thereby promoting the accumulation of aggregating proteins and/or activating senescence-inducing signalling pathways. Main Objectives: The main objective of this proposal is to determine whether, and how, the accumulation of spuriously spliced transcripts leads to cellular senescence. We will address this through the following specific aims: 1. To determine how the degradation and nuclear export of spuriously spliced RNAs are altered in human senescent cells. 2. To assess the capacity of aberrantly spliced transcripts to trigger cellular senescence. 3. To identify changes in the activity and localization of RNA quality control and RNA processing factors in human senescent cells. 4. To define the impact of defective RNA quality control and processing factors on proteostasis and cellular signalling. Methodology: We will employ proliferative and senescent non-transformed human diploid skin fibroblasts, available in my laboratory. Changes in the degradation rate and nuclear export of spuriously spliced RNAs and their properly spliced counterparts (Aim 1) will be assessed by real-time quantitative PCR (qPCR) following transcriptional inhibition, and single-molecule FISH, respectively. To evaluate the ability of aberrantly spliced transcripts to induce senescence (Aim 2), we will overexpress NMD targets or control RNAs via viral transduction. Senescence induction will then be assessed using established markers, including changes in cell morphology, β-galactosidase staining, and quantitative PCR. Changes in the RNA-binding activity and subcellular localization of

RNA quality control and processing factors during senescence (Aim 3) will be examined using RNA-interactome capture and fluorescence microscopy, respectively. Finally, to define the cascade of events linking splicing defects to senescence (Aim 4), we will assess the impact of partial pharmacological inhibition of the splicing machinery on the accumulation of aggregated proteins using anti-ubiquitin immunofluorescence and evaluate changes in cellular signaling through phosphoproteomic analysis.

Lay Summary / Impact of the Study:

Cells are constantly engaged in a never-ending telephone game, where genetic information is passed from DNA to RNA to protein. For cells to stay healthy, this flow of information must be precise and tightly regulated. One crucial step in this process is called “splicing,” which ensures that the correct RNA molecules are produced by stitching together the proper parts of a gen. As we get older, the splicing process becomes less accurate. This can cause cells to enter a state called senescence—a kind of "zombie" state where cells stop performing their normal functions but continue to secrete inflammatory molecules that damage surrounding tissues and contribute to aging and disease. How splicing errors trigger senescence is still not well understood. In this project, we aim to study this process using human skin cells grown in laboratory dishes. Understanding how splicing defects lead to cellular senescence may reveal new ways to control the accumulation of these cells in our bodies as we age, potentially helping to slow age-related decline and prevent age-related diseases.

Host lab at GIMM:

Joel Perez-Perri, RNA Regulation and Aging (https://gimm.pt/lab/joel-perez-perri-lab/)

External Collaboration:

Dr. Ina Huppertz, Max Planck Institute for Biology of Ageing, Germany

Expected duration of the external collaboration:

1 month

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Project #3

Title:

Targeting immune-stem cell interactions in aging to restore organ health

Description:

A central promise of regenerative medicine is the extension of human health span through the use of stem cells to repair and rejuvenate aged organs. Nevertheless, the clinical success of such therapeutic approaches is limited by the inefficient repair capacity of old, degenerating tissues. Although inflammatory pathways are essential regulators of regeneration, age-associated alterations to the immune environment constitute a major roadblock to the successful transplant of stem cells for tissue repair in old organs. Thus, restoring immune-stem cell communication in aging is a promising strategy to improve regenerative success. However, which specific defects in the immune signalling should be targeted by these interventions remains elusive, mostly due to our poor understanding of the basic principles of immune dysregulation during tissue repair in aged organisms.

Our lab applied a combination of single cell transcriptomics, bioinformatic tools and functional studies to identify novel nodes of immune-stem cell communication that are disrupted in aged animals and can represent new targets for intervention. In this project the student will use skeletal muscle regeneration in aged mice and genetic models of age-related immune alterations to test the relevance of these novel candidates to improve stem cell activity and regenerative capacity in aging. The project will combine flow cytometry, histological assessment of tissue structure and analysis of multi-omic data to assess the therapeutic efficacy of selected molecules. The analysis of candidate molecules can involve a working period in an international lab, in the context of on going collaborations.

By uncovering the roadblocks imposed by immune aging to the success of regenerative therapies, this research aims to pave the way for more effective stem-cell based treatments to rejuvenate aged organs, extending the healthy years of our elderly population.

Lay Summary / Impact of the Study:

Stem cells hold tremendous promise for extending healthy human lifespan by repairing and rejuvenating aged organs. These master repair cells can transform into any type of tissue needed to fix damage throughout the body. However, stem cell therapies often fail in aged individuals because aging organs don't respond the same way as younger ones. One key reason is that the immune system, which plays an important role in healing, changes with age and can actually interfere with the repair process instead of helping it. Our project

explores how aging affects the communication between the immune system and stem cells. Using cutting-edge technologies like single-cell analysis and genetic models in mice, we are identifying specific changes in the immune system that disrupt healing in aged organs. We are then testing new ways to restore this lost communication and boost the ability of stem cells to regenerate these same organs. By uncovering the hidden immune barriers to successful healing in aging, this research aims to pave the way for more effective regenerative treatments that improve the function of aged organs, extending the healthy years of our elderly population.

Host lab at GIMM:

Neves & Sousa-Victor, Aging & Tissue Repair (https://gimm.pt/lab/neves-sousa-victor-lab/)

External Collaboration:

To be determined later.

Expected duration of the external collaboration:

To be determined later.

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Project #4

Title:

AGEWISE: Unravelling the Gut-Hormone Axis in Women's Ageing

Description:

During the menopausal transition, women face an increased risk of age-related chronic diseases, including cardiovascular disease, cancer and diabetes. This subject necessitates a thorough exploration of the underlying mechanisms driving these health challenges, often triggered by a decrease in ovarian sex hormones like estradiol after menopause. Preliminary research suggests a potential link between menopause and shifts in the gut microbiota, implicating hormonal and physiological changes. Gut bacteria metabolise oestrogen, influencing the hormone's circulating forms within the body. These gut bacteria are susceptible to modulation through lifestyle choices such as dietary habits, which could, in turn, affect the risk of diseases more common in women after menopause. The post-menopausal dysbiosis induced by hormonal fluctuations is thought to contribute to physiological alterations, emphasising the need for further research to elucidate the microbiome's role in disease risks associated with menopause. However, little is known about the influence of menopause on the gut microbiome. Many gaps in knowledge remain, including the role the gut microbiome may play in menopause-related disease risks. AGEWISE aims to fill critical gaps in our understanding of the intricate interplay between menopause, the gut microbiome, and female sex hormones. This project endeavours to revolutionise the early detection and proactive management of conditions commonly linked to menopause by leveraging personalised risk assessments. Through AGEWISE, we strive to advance women's health during the ageing process, representing a crucial step toward transformative insights and enhancements in understanding and promoting the well-being of women navigating the complexities of menopause.

Aims

Aim 1: Characterise Taxonomic and Functional Changes in the Gut Microbiome

1.1: Identify and catalogue taxonomic shifts in the gut microbiome of pre-, peri-, and postmenopausal women through comprehensive metagenomic analysis.

1.2: Examine functional changes in the gut microbiome during different stages of menopause, correlating these with hormonal variations.

Aim 2: Identify Hormonal and Inflammaging Blood Biomarkers

2.1: Quantify hormonal fluctuations in pre-, peri-, and postmenopausal women through extensive blood biomarker analysis.

2.2: Investigate inflammaging biomarkers to understand their association with hormonal changes during menopause.

Aim 3: Develop a Microbiome-based AI Platform

3.1: Create a comprehensive database integrating microbiome data, clinical records, lifestyle, and dietary information of women in different menopausal stages.

3.2: Design and train an AI algorithm capable of predicting individualised risks for menopausal-associated conditions based on integrated data.

This project has received seed funding from the Biocodex Foundation.

Lay Summary / Impact of the Study:

As women age, they go through menopause - a natural but significant transition that marks the end of reproductive years. This stage is often accompanied by a drop in oestrogen levels and an increased risk of age-related health problems such as heart disease, osteoporosis, diabetes, and cognitive decline. While these changes have traditionally been seen as a normal part of ageing, new research suggests that the gut microbiome may play a key role in how women age and how healthy they remain in later life.

The AGEWISE project is exploring how changes in gut bacteria during menopause may influence long-term health and the ageing process. By studying 300 women at different stages of menopause, AGEWISE will track changes in gut bacteria, hormone levels, and markers of inflammation in the body. The project will also collect detailed information about diet, lifestyle, and overall health. All this data will feed into a cutting-edge artificial intelligence (AI) platform designed to assess individual health risks and provide personalised recommendations.

AGEWISE's ultimate goal is to support healthier ageing and longer, more active lives for women by identifying early warning signs of menopause-related diseases and suggesting lifestyle changes that can help prevent them. By deepening our understanding of the links between menopause, the gut microbiome, and healthy longevity, this project aims to transform how we approach women's health in midlife and beyond - paving the way for more informed, proactive care as women age.

AGEWISE seeks to address critical gaps in our understanding of the intricate relationship between menopause, the gut microbiome, and female sex hormones. Through the development of innovative microbiome-based diagnostic tools, it holds the potential to significantly enhance women's health. The project's ultimate goal is to harness the power of

AI to transform an individual's biological and lifestyle data into a personalised and predictive menopause-related risk profile. This approach may pave the way for creating and implementing lifestyle changes in the future to prevent or delay age-related morbidities in menopausal women. Given that approximately 50 million women enter menopause annually, exhibiting reduced oestrogen levels and heightened inflammatory markers associated with brain, bone, and heart diseases, this research is pivotal. The project's cornerstone will be a robust, intuitive AI system that gathers biological and lifestyle information, generating individualised risk assessments for menopause-related conditions.

Host lab at GIMM:

Ana Santos Almeida, Microbiome in Health & Disease Translational Laboratory (https://care.gimm.pt/lab/microbiome-in-health-disease-translational-laboratory/)

External Collaboration:

Dr. Siobhain O'Mahony, APC Microbiome Ireland, University College Cork, Ireland

Expected duration of the external collaboration:

1 month