Projetos Xperience 2022

Projeto	1	2	3
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Área Científica Principal	Ciências Sociais	Ciências Médicas e da Saúde	Ciências Médicas e da Saúde
Área Científica Secundária	Psicologia	Ciências da Saúde	Ciências da Saúde
Título	Volunteering in mental health	How and why does our brain age? Using zebrafish as a model to decipher the interplay between senescence and inflammation in the ageing brain and the potential role of telomerase	Determining the role of Pex30-like proteins in the formation of membrane contact site between endoplasmic reticulum and peroxisome
Data de início do projeto	1/6/2022	1/6/2022	4/7/2022
Sumário	Volunteering in mental health programmes has been created to provide support for patients in mental health care. The provision of this resource involves two main stakeholders: mental health professionals, who may encourage or prescribe volunteering to their patients; and volunteers, who provide the volunteering support. Despite stakeholders' key roles, little is known about their views on these mental health volunteering programmes regarding their availability in terms of provision and delivery. This project will analyse data collected from a large focus group study conducted in different European countries, including Portugal, to ascertain the views of stakeholders in Portugal who may be involved in the provision of volunteering, i.e. mental health professionals and volunteers. Focus groups generate a wide set of data by its nature and are a particularly well-suited approach for under researched topics. The current project will conduct a secondary qualitative analysis focusing on the data from the focus groups conducted in Porto. In total, six transcripts will be analysed from the four focus groups conducted with mental health professionals, and the two focus groups with volunteers. Inductive thematic analysis will be used to analyse this dataset. Secondary analysis serves to use existing research data to answer a new research question and generate new knowledge. Within qualitative research, it is an emergent methodology which is generally underused. It can however offer an opportunity to expand on existing research data. As the aims of the primary study were to focus on emergent themes across European countries rather than in a specific country or between stakeholders, there may have been themes in the Portuguese dataset which were not reported, which a secondary in-depth analysis focusing on the data of one setting only could uncover.	We work together to answer difficult questions regarding how cells interact within tissues throughout life and, in particularly, how the immune system changes with ageing and stops doing what is supposed to do. We use zebrafish as a model, because I have shown that zebrafish share key aspects of human ageing, particularly in what concerns telomere maintenance. We have particular interests in how the gut ages and how it communicates with the brain and, in turn, how this affects how the whole organisms ages and develops disease. Brain ageing and related neurodegenerative diseases have dramatic consequences in quality life as well as medical care costs in elderly and, therefore, it is urgent to understand the mechanisms underlying it. Decreased telomerase expression, senescence-associated markers and inflammation have all been independently observed in the ageing brain and associated with disease. Senescence cells are non-proliferative but metabolically active, realising several factors, including pro-inflammatory molecules, that can damage and promote inflammation in the surrounding tissue. Importantly, accumulation of senescent cells has been associated with several age-related diseases. However, causality between limited telomerase expression and increased senescence in the natural ageing setting, and whether these drive neuro-inflammation is yet to be established. This project aims at establishing whether there is a telomerase-dependent increase in senescence and inflammation in the ageing brain. We also aim to determine if inflammation influences the accumulation of senescence or vice-versa. This project is part of ongoing work in the lab and it will provide key data for a publication and future grant applications, aiming at identifying therapeutic strategies to prevent or ameliorate ageing and age-associated neurodegeneration and disease in the brain.	Lipid metabolism requires tight coordination between distinct intracellular organelles, which results in metabolic disease when dysregulated. De novo assembly of key organelles, such as lipid droplets (LDs) and peroxisomes, is highly dependent on the endoplasmic reticulum (ER) that produces membrane lipids and proteins. Lipid droplets are ubiquitous organelles responsible to store intracellular lipids, while peroxisomes are responsible for fatty acid oxidation – an essential step in lipid consumption. The growth and maturation of these organelles is supported by ER-derived lipids transferred at membrane contact sites (MCS). MCS correspond to areas of close apposition between membranes of two organelles, allowing exchange of molecules without their fusion. MCS are extremely dynamic, and their formation, regulation, and function are still poorly understood. Answering these questions may reveal new targets for therapeutics of metabolic diseases. Recently, we found that proteins of Pex30-family, first characterised as important during peroxisome biogenesis, form distinct complexes that the localise at different MCS: ER-LDs, ER-peroxisomes, and ER-vacuole. The absence of Pex30-like proteins results in aberrant morphology and function of these MCS and organelles. However, how these proteins mechanistically contribute to the formation of these MCS is unclear. To complement these exciting observations, I propose to supervise the selected student in utilising genetic tools using yeast as model system to characterise the formation of MCS in absence of the Pex30-family proteins. This work will involve knocking out, fluorescently-tag or mutating genes of interest and the use of live cell microscopy to analyse protein localisation and general change in organelle phenotype. The role of these proteins during biogenesis of new peroxisomes will also be explored, which will allow the student to optimize a system to evaluate peroxisome morphology in yeast. This project will significantly contribute to our understanding of how the Pex30-like proteins contribute to the formation of the MCS and how it affects the function and formation of new peroxisomes.

Objetivos do Projeto	The overarching aim of this project is to explore the views of two main stakeholders: mental health professionals and volunteers in Portugal, on the provision of volunteering in mental health care. The study objectives are: 1) To compare the views of mental health professionals and volunteers in Portugal on volunteering within mental health care, 2) To explore the views of mental health professionals in Portugal on the role which volunteering should play within mental health care. Comparing the views of different stakeholders can serve to inform the provision of volunteering interventions. The researcher who will be contributing to this project will acquire knowledge and skills on qualitative research. This will include following the six phases of thematic analysis as outlined by Braun and Clarke (2006), namely: familiarisation with the data, generating initial codes, searching for themes, reviewing themes, defining and naming themes and producing the final write up. The qualitative software NVivo version 12 will be used to code and analyse transcripts. This software allows for the easy storage and retrieval of the data.	Determine levels of inflammation and senescence in the gut and brain before and after therapeutic manipulation of either process. The student will be performing immunofluorescence staining and image processing and quantification of specific immunofluorescence staining in zebrafish brain sections. The student will be taught how to perform immunofluorescence in tissue sections and how to use ImageJ, Excel, GraphPad prism and Illustrator to process, analyse, quantify and present data in the form of figures suitable for publication. Basic statistical training will also be provided, as well as general scientific thinking, hypothesis testing and immunofluorescence analysis. The student will also get a basic training on the anatomy of the brain and specific cellular and molecular mechanisms of ageing.	This project aims to characterise the contribution of Pex30-family proteins on the formation of MCS between the ER and the peroxisome in Saccharomyces cerevisiae. Specifically, I will teach the student how to: 1) Prepare culture medium and working solutions. 2) Grow yeast cells for distinct experimental approaches. 3) Genetically modify yeast by different methods (genomic integration, CRISPR/Cas9 and yeast crossing) to express fluorescent labelled proteins or delete genes of interest. 4) Evaluate protein expression by SDS-page and Western blotting. 5) Perform live imaging of fluorescently labelled yeast. 6) Analyse microscopy data. 7) Prepare a short oral presentation to the research group about the findings of the work. During this internship the student will also interact and learn about other research being done in the laboratory, including work on mammalian cell lines, biochemistry, and structural biology. The student will have the opportunity to participate in the group's weekly meetings and departmental seminars (given by world renowned speakers). At the end of this internship, the student will have gained high-quality laboratory experience and be able to transfer many of the skills across other model organisms and scientific questions.