FOIE GRAS ITN – 722619

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The Bioenergetic Remodelling in the Pathophysiology and Treatment of Non-Alcoholic Fatty Liver Disease (FOIE GRAS) project seeks to answer two critical, yet unanswered questions. It is expected that the findings from the project could lead to reversing the burden of non-alcoholic fatty liver disease, thereby advancing the health and wellbeing of European citizens

Non-alcoholic fatty liver disease (NAFLD) is characterised by fatty infiltrations in the liver that have not been caused by alcohol consumption. Over time, NAFLD can lead to non-alcoholic steatohepatitis (NASH), which is a more serious stage of the disease. It results in an inflamed liver due to the accumulation of fat and represents a significant health burden around the world. Indeed, guidelines published in 2012 by the World Gastroenterology Organisation, suggest the prevalence of NAFLD has doubled over the last 20 years, with both NAFLD and NASH being closely associated with type 2 diabetes and obesity. Together, they are regarded as the primary cause of liver disease in Western countries. Studies show that in 2013, 29 million people in the European Union suffered from a chronic liver condition. NAFLD is predicted to become the primary cause of liver transplants by 2020 and therefore represents a potential major threat to public health systems in Europe and the world in general. Thus, NAFLD represents a significant economic and health burden in Europe. Understanding more about the mechanisms behind it is a significant topic of interest for scientists and researchers across Europe.

Integrating Expertise with Training

With that in mind, the FOIE GRAS project has been established. Led by the Principal Investigator Professor Paulo Oliveira, this four-year Horizon 2020 project began in January 2017 and focuses on providing innovative training for 13 Early Stage Researchers (ESRs). A crucial aspect of the project is the attempt to answer two critical, and as yet unanswered questions. First, is hepatic bioenergetic remodelling involved in NAFLD pathogenesis, and a target for stratification or therapeutic/lifestyle interventions? Second, is the disruption of the gut-liver axis involved in NAFLD progression? One of the particularly exciting aspects of the project is that it combines strong scientific expertise with integrated and complementary training. Specific factors include translational research, clinical practice, technology commercialisation and public outreach. Partnering with industry is seen as crucial to the success of the project, where microBiolytics and Mediagnost help provide experience on commercialising the findings from FOIE GRAS, while the affiliated patient organisation, APDP-ERC, will provide important training related to societal awareness topics. Agilent, which acquired Seahorse Biosciences, will

CNC – Center for Neuroscience and Cell Biology
University of Coimbra
UC Biotech Building, Lot 8A, Biocant Park
3060-197 Cantanhede, Portugal

Tel: (+351) 231 249170
Fax: (+351) 231 249 179
coordinator.etnfoiegras@cnc.uc.pt

provide training regarding metabolic technological platforms. However, perhaps the most unique aspect of FOIE GRAS is its keen focus on training ESRs. 'ESR training utilises network-wide workshops and secondments to foster translation of basic research to clinical applications and SME creation,' explains Oliveira. 'This diverse yet integrated skill set enhances the employment prospects of the trained researchers in both academic and non-academic sectors.' Importantly, the FOIE GRAS network embraces the Marie Skłodowska-Curie ETN action in training ESRs with transferable skills. In doing so, Oliveira and his team hope to boost the individual ESRs' career development and long-term opportunities, as well as maintaining a level of interest in NAFLD research.

Widespread collaboration for wide-ranging success

It is the team's belief that NAFLD pathogenesis and progression involves nutrient, inflammatory and oxidative stress factors that directly or indirectly impair metabolic activity and energy generation in the liver. Thus, successfully characterizing the underlying mechanisms or metabolic and gut-liver axis dysfunction, identifying biomarkers that inform metabolic status, and designing interventions for restoration of normal metabolic activity in NAFLD patients are the main goals of this project. To address these goals, there needs to be a clear focus on the need for collaboration, not only because it is vital that new methods and training move away from current practice; but also because collaboration helps foster this new form of approach. 'At present, the typical training in the field of liver diseases is limited to specific aspects, usually not providing interaction with basic, clinical and industrial fields. Generally, academic and non-academic sectors work separately to provide their own direction to ESRs, with collaborative opportunities being bound to a narrow scope,' explains Oliveira. 'FOIE GRAS introduces a well-balanced, pan-European structure to support the career development and training of researchers. FOIE GRAS partners consistently match the proposed research topics across academic and nonacademic sectors in Europe and have a record of previous successful collaborations between themselves.' Indeed, the supervisors and co-supervisors involved in the project are all renowned researchers in their particular areas of expertise, and have substantial experience in heading national and international research projects. This puts them in a perfect position to effectively manage the respective areas of study and ensure the project remains focused on independent, but entirely complementary investigations.

Right tools for the job

While bringing 13 ESRs together to work towards producing improved understanding and clinical outcomes for NAFLD is of great importance, it is equally important that these individuals are given the tools they need to flourish and advance in their careers. Accordingly, FOIE GRAS provides access to top facilities and modern equipment, often through partnering with various industries. In addition, it provides a mean for metabolic analyses in cells in culture

and isolated mitochondrial fractions, as well as high-precision respirometry, there are also provisions for nuclear magnetic resonance facilities, microscopy and genomics/proteomics. Alongside the technologies that will be employed, Oliveira is keen that the ESRs are imbued with some societal qualities that are essential for effective research. 'We will help the 13 individuals by getting them to work alongside patients, clinicians and industry,' explains Oliveira. 'An important objective of one of the 13 ESR projects is to develop and implement strategic communication and educational activities addressing NAFLD awareness, which targets the general public and aims to inform and promote healthy lifestyles.'

Sowing the seeds of success

Given the project only began in January 2017, and the time it took to identify the 13 ESRs who would form part of FOIE GRAS, there have been no true scientific results as yet. However, there has been evidence of progress to date, even at this early stage. Building bridges between different research groups is no mean feat, while bringing various people together to discuss science – as well as identifying and hiring the best researchers for the job – are essential seeds for the successful germination of the FOIE GRAS project. Ultimately, Oliveira and his colleagues hope to clearly identify and validate the biomarkers involved in NAFLD, which will naturally lead to accurate diagnosis, effective treatments and effective tools to monitor disease response. Together, these will help improve support for medical practice. Of equal importance is putting together an educational package that will encourage individuals to lead healthier lifestyles, modify their behaviours and significantly reduce the burden that NAFLD currently represents. As the science behind understanding NAFLD improves, so will the understanding of individuals. And with 13 ESRs becoming well-versed in every aspect of NAFLD, it is reasonable to expect an even brighter future for those individuals and NAFLD patients.

Project Insights

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Participants

Dr Paulo Oliveira – Centro de Neurociencias e Biologia Celular (CNBC), Portugal
Dr Jan Kopecky and Dr Martin Rossmeisl – Fyziologicky Ustav Akademie ved Ceske Republiky (IPHYS), Czech Republic
Dr Piero Portincasa – Universita Degli Studi di Bari Aldo Moro (UNIBA), Italy
Dr Cecilia Rodrigues – Faculdade de Farmácia da Universidade de Lisboa (FFUL), Portugal

Dr Mariusz Wieckowski – Instytut Biologii Doswiadczalnej Im M Nenckiego Polskiej Akademii Nauk (NENCKI), Poland
Dr Fernanda Borges and Dr José Magalhaes – Universidade Do Porto (UPORTO), Portugal
Dr Carina Prip-Buus – Institut National de la Sante et de la Recherche Medicale (INSERM), France
Dr Amalia Gastaldelli – Institute of Clinical Physiology of the National Research Council (IFC-CNR), Italy
Dr Hans Zischka – Helmholtz Zentrum Muenchen Deutsches Forschungszentrum Fuer Gesundheit und Umwelt GmbH (HMGU), Germany
Dr Joan Catafau – Agencia Estatal Consejo Superior Deinvestigaciones Cientificas (CSIC), Spain
Dr Paula Macedo – Associação Protetora dos Diabéticos de Portugal (APDP), Portugal
Dr Martin Winter – micro-biolytics GmbH, Germany
Dr Andrea Normann – Mediagnost Gesellschaft Fuer Forschung und Herstellung von Diagnostika GmbH, Germany

CONTACT

Professor Paulo Oliveira
Principal Investigator and Invited Assistant Professor
T: +351 231249195
E: pauloliv@cnc.uc.pt
W: www.projectfoiegras.eu

Liljana Georgievska
Project Manager
E: liljana.georgievska@cnc.uc.pt

PRINCIPAL INVESTIGATOR BIO

Professor Paulo Oliveira completed his PhD in Cellular Biology in 2003 at University of Coimbra, Portugal. He is currently head of the Mitochondrial, Metabolism and Disease Workgroup and the Principal Investigator at the MitoXT: Mitochondrial Toxicology and Experimental Therapeutics, both at CNBC. His main research interests involve the role of mitochondrial biology in metabolic diseases and cancer, drug-induced mitochondrial dysfunction, and the development of mitochondrial-targeted molecules that can delay metabolic disruption during different pathologies.

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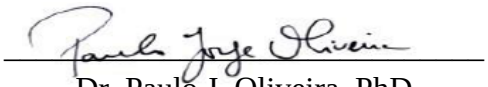

Dr. Paulo J. Oliveira, PhD
(Project Coordinator)

CNC – Center for Neuroscience and Cell Biology
University of Coimbra
UC Biotech Building, Lot 8A, Biocant Park
3060-197 Cantanhede, Portugal

Tel: (+351) 231 249170
Fax: (+351) 231 249 179
coordinator.etnfoiegras@cnc.uc.pt