Strategic projects

Amniogel – Extracellular matrix derived products from human placenta to engineer bone microtissues for in vitro disease models 18 months; € 150K

The research team led by João F. Mano, full professor from the Department of Chemistry, and researcher at CICECO – Aveiro Institute of Materials, has been awarded for the second time with a Proof of Concept grant by the European Research Council (ERC-PoC). This grant, created to support ideas with commercial potential capable of achieving economic or social benefits will provide the team with 150,000 euros to develop the AMNIOGEL project during 18 months.

Based on the knowledge that resulted from the ERC Advanced Grant (ERC-AdG) ATLAS, the goal of this project is to develop highly personalized osteosarcoma microtissues for in vitro disease modelling and drug screening. Osteosarcoma is a rare but devastating bone tumor very resistant to therapy, that mainly affects children, adolescents and elderly. In AMNIOGEL the research team will use proteins obtained from perinatal tissues, namely the amniotic membrane, that is normally discarded after childbirth. The proteins are used to prepare fully human based biomaterials that will support cell culture and mimic the tumor microenvironment. The human based nature of the biomaterials proposed in AMNIOGEL will improve the predictive value of the effect of anticancer drugs, accelerating new therapies development. AMNIOGEL will address current challenges in 3D cell culture with human protein based products as substrates that do not require extra functionalization steps that can be time consuming and costly, are mechanically tuneable and do not carry associated animal contamination issues and ethical concerns being also versatile and easy to manipulate.

The project could have a considerable impact, as the proposed innovative products for cell culture have the capacity to replace animal testing, accelerating drug screening and reducing associated costs.



This project has received funding from the European Union Horizon 2020 – ERC, under grant agreement ID: 957585

More information https://cordis.europa.eu/project/id/957585 **REBORN: Full human-based multi-scale constructs with jammed regenerative pockets for bone engineering.** $60 \text{ months}; \in 2.5M$

Advanced Grants from the European Research Council (ERC-AdG) are awarded after the application in extremely competitive calls, in which the unique evaluation criterion is the scientific excellence. The assessment includes the analysis of the scientific track record of the researcher, which must be at the top level of researchers working in Europe, as well as the quality of the project to be carried out, its degree of risk and the radically innovative approach adopted in the proposed work programme.

João F. Mano, full professor from the Department of Chemistry, and researcher at CICECO – Aveiro Institute of Materials, has been awarded, for the second time in a row, with such a prestigious grant.

The ERC-AdG grant will allow, for 5 years, to develop cutting-edge work in the field of bioengineering of human tissues and advanced biomaterials, namely in the creation of strategies for the regeneration of bone tissue, which may have a clinical impact in cases of massive loss or extensive bone fractures. One of the innovations of the project is the use of proteins obtained from tissues collected during childbirth, normally disposable, namely the amniotic membrane and the umbilical cord. These will serve as a basis for the construction of highly hierarchical devices, from the nano-scale to the macroscale, with a high capacity to generate mineralized bone tissue and promote its vascularization. From these perinatal tissues it will be also possible to collect and use cells that will play a fundamental role in the construction of tissues in vitro. The cells will be encapsulated into small artificial "placentas" that will provide appropriate biochemical and mechanical signals and will promote the formation of functional micro-tissues in a completely autonomous manner. The agglomeration of these "regenerative pockets" in a controlled spatial way will allow the development of three-dimensional tissues at the scale-length of real bone defects, with high geometric precision.

In addition to direct therapeutic applications involving implantation, these innovative devices may also serve as models of diseases with dimensions and specifications similar to those of real tissues, in order to test new drugs and therapies; those can be seen as an alternative solution to animal tests or clinical trials.





Chemistry tools+ advanced bioengineering —

This project has received funding from the European Union Horizon 2020 - ERC, under grant agreement ID: 883370

More information https://cordis.europa.eu/project/id/883370

EpiViral – Viruses and Epitranscriptomics: seeking novel targets for antiviral therapy

36 months; € 878K

EpiViral is a Coordination and Support Action (CSA) – Twinning – from the H2020 program, aiming at intensifying, increasing and consolidating the scientific research on Virology and RNA-modification biology (epitranscriptomics) at the Institute of Biomedicine, University of Aveiro (iBiMED-UAVR), by partnering with two leading institutions in these research fields, namely the Leiden University Medical School (LUMC) and the Goethe University Frankfurt (GUF).

Viral infections are one of the most prominent and persistent threats to human health, resulting in high mortality rates and tremendous impact on the economy. The frequent mutations and common emergence of new viral species undermines a large part of the existing therapeutics, which are mainly directed at specific viruses or strains, and emphasizes the importance of the discovery of novel broadspectrum antiviral combat strategies. The EpiViral consortium believes that the basis for such therapeutics may be unraveled by investigating common mechanisms shared by different viruses, e.g. as part of their life cycle or interaction with their host cells. More specifically, EpiViral is committed to study how the host epitranscriptome, in particular the tRNA epitranscriptome, is regulated upon infection and how it can eventually be manipulated for antiviral therapy. As viruses are completely dependent on the host-cell translation machinery to translate their own genomes, they have to efficiently hijack host tRNAs, which are the effector molecules of translation. However, host tRNA pools are optimized to efficiently recognize and translate host mRNAs and not viral mRNAs. The EpiViral consortium hypothesizes that, upon infection, viruses reprogram host tRNA modification patterns to facilitate viral mRNA translation. The EpiViral consortium aims at enabling a series of state-of-the-art studies to further understand virus- and host-mediated tRNA epitranscriptomic changes and its regulation during infection, as well as to evaluate the host epitranscriptome as a new therapeutic target against viral infections.

EpiViral will coordinate and promote networking activities between all the partners, knowledge dissemination and transnational access of iBiMED-UAVR researchers to state-of-the art infrastructures available at LUMC and GUF.

EpiViral will be pivotal to place iBiMED-UAVR at the forefront of stateof-the-art research on the interface of virology and epitranscriptomics.



This project has received funding from the European Union Horizon 2020, under grant agreement ID: 952373

More information

https://cordis.europa.eu/project/id/952373 www.epiviral.eu

KleptoSlug – Kleptoplasty: The sea slug that got away with stolen chloroplasts $60 \text{ months}; \in 2.2M$

KleptoSlug is an European Research Council (ERC) funded project to resolve some of the long-standing questions regarding the maintenance of photosynthetically active chloroplasts in animal cells and produce crucial insights about long-term kleptoplasty in sacoglossan sea slugs.

Photosynthesis is almost exclusively restricted to algae and plants, with the exception of some protozoans, flatworms and marine slugs that acquire chloroplasts from algae. In metazoans, the capacity to incorporate functional chloroplasts (kleptoplasty) for long periods of time has only been described in sacoglossan sea slugs. Some species retain kleptoplasts photosynthetically active for several months that persist without access to algal gene products and despite the release of potentially dangerous metabolites, including reactive oxygen species. While kleptoplasty is intriguing from an evolutionary perspective, there are many unresolved questions on how the algal organelle is incorporated into the metabolism of an animal cell and what the host-associated benefits are. This proposal aims at unravelling the cellular mechanisms supporting the sequestration and maintenance of functional chloroplasts inside metazoan cells and determining the host benefits of harboring kleptoplasts. The project will compare a wide range of different animal-alga associations in their response to chloroplast incorporation and variable ability to functionally maintain them. Lipidomic and transcriptomic analyses will unravel in a comparative approach the species-specific maintenance strategies underlying kleptoplasty. In addition, the impact of cytotoxic compounds produced by active kleptoplasts, in particular the reactive oxygen species accumulated due to photosynthesis and respective scavenging, will be explore. Finally, the project will determine the fate of inorganic carbon and nitrogen in the animal metabolism to explore the contribution of photosynthesis-derived compounds to the physiology of the host. New equipment, such as gas chromatography combustion isotope ratio mass spectrometry (GC-IRMS), will be implemented at the University of Aveiro/CESAM for highly specialised analysis of the relative ratio of light stable isotopes of carbon (13C/12C) and nitrogen (15N/14N) in individual compounds.



KleptoSlug summary. Five model species with variable capacities for retention of functional chloroplasts will be used to address in a comparative and in depth approach the main molecular interactions between host and kleptoplasts. The project comprises 3 workpackages: The perfect match – Unravel sacoglossan mechanisms to maintain functional chloroplasts (WP1); Living with the enemy – Linking reactive oxygen species (ROS) to kleptoplastidic abilities (WP2); and Stashing the loot – Determining the benefits of kleptoplasty (WP3).

This project has received funding from the European Union Horizon 2020 -ERC, under grant agreement ID: 949880

More information https://cordis.europa.eu/project/id/949880 http://www.cesam.ua.pt/index.php?menu=&language=pt&tabela=projectos detail&projectid=1681

PurelgY-Towards the use of IgY antibodies as alternative therapeutics

18 months; € 150K

Thanks to European Research Council (ERC) with the funding scheme of ERC-POC-LS, activities developed by researchers already awarded with a previous ERC grant can be supported to address their commercial and societal potential. Based on the knowledge acquired and technology developed during the ERC Starting Grant IgYPurTech, Dr. Mara G. Freire and her team, from CICECO-Aveiro Institute of Materials and the Department of Chemistry of University of Aveiro, have been working in the scope of the ERC-PoC PurelgY to apply immunoglobulin Y (IgY) antibodies as alternative therapeutics to tackle the antimicrobial resistance (AMR) scenario. Despite the wide therapeutic applications of IgY antibodies, the research team is dedicated on using the developed innovative IgY purification platform to create therapies for antimicrobial-resistant pathogens since they are an economic and societal challenge of high priority. AMR is responsible for 33,000 deaths per year, bringing €1.5 billion per year in healthcare costs and productivity losses to the EU. Novel alternatives to antibiotics are highly expensive or are in a very earlystage of development. Therefore, low-cost and relatively low timeto-market alternative therapeutics must be pursued.

IgY, present in hen's egg yolk, is a potential alternative to antibiotics that can be obtained by a non-invasive method at high amounts from a renewable matrix. However, given the complex nature of egg yolk, the current purification technologies are multi-step and mainly based on chromatography, which are highly expensive and lead to low yields. Within the IgYPurTech framework an innovative and cost-effective platform to purify IgY was developed, enabling the production of high-quality IgY in higher amounts and significantly lower cost than other currently commercialized biotherapeutics. In the PureIgY PoC Action it is aimed to scale-up the developed purification technology, to address the biological features of specific IgY from hyperimmnune eggs to tackle the AMR critical scenario, to work on the business plan development and business development, and to create an early-stage drug development start-up (RYAPURTECH, created in March 2020).



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More information https://cordis.europa.eu/project/id/899921

SMART-ER – The ECIU University Research Institute for Smart European Regions

36 months; € 1,99M; 12 Partners

The ECIU University Research Institute for Smart European Regions (SMART-ER) is a research, innovation and education strong alliance, enabling all 12 member universities to jointly address complex societal challenges under the framework of the UN SDG11 (Make cities inclusive, safe, resilient and sustainable), identified by the ECIU University.

Along 36 months, SMART-ER will design, develop and implement research, value-capture and deliver solutions to current and future UN SDG11 challenges. Activities will be implemented by bringing together scientific and management research capacities at the member institutions in a challenge-based approach.

Together with diverse stakeholder groups at a local, national and international level, SMART-ER will work according to a shared Research and Innovation Agenda. Jointly, the institutions will pilot capacity building programmes (Seed Programme and SMART-ER Academy) and citizen science initiatives that will be used as a testbed to put into practice all the mechanisms and structures built.

Strategic SMART-ER initiatives

- . Develop a common research and innovation agenda and convergence action plan, sharing infrastructures and resources, in synergy with education strategies and regional engagement.
- . Develop and implement strategies for strengthening human capital and collaborations in research and innovation.
- . Embed citizens and society, involving and engaging citizens, civil society and authorities in research and innovation.

The SMART-ER Research Institute will implement a new research and innovation model without walls while promoting the dialogue with society, overcoming the limitations of disciplines, sectors and countries, based on a virtual collaborative environment.

https://cordis.europa.eu/project/id/101016888

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