**GROUP'S NAME:** (sugere-se que o nome fique a 2 linhas, no máximo 3 linhas – 57 caracteres, sem espaços)

**CANCER BIOLOGY & EPIGENETICS GROUP**

## PROJECTS WITH EXTERNAL FUNDING

### INTERNATIONAL

**EURECA – "The European Epitranscriptomics of Cancer Academy Description"** Funding agency: European Commission HORIZON-MSCA-2024-DN-01(Grant agreement ID: 101226733), Budget: 243K€ (2025-2029) [PI@IPO Porto: Prof. Carmen Jerónimo, Coordinator- Dr Elena Martens-Uzunova (ERASMUSMC, NL)].

EURECA aims to train a new generation of doctoral candidates in cutting-edge basic and translational research by exploring the cancer epitranscriptome to address unmet clinical needs in diagnosis, prognosis, and therapy. Epitranscriptomics, the study of chemical modifications on RNA that regulate gene expression, has emerged in the past decade as a crucial field revealing how RNA modifications impact cell behavior and contribute to cancer development. Recognising these modifications as a new hallmark of cancer, EURECA focuses on RNA methylation and RNA editing across three cancer types to uncover shared and distinct epitranscriptomic patterns, identify new biomarkers, and develop novel treatment approaches. Through a collaborative network of top-tier European academic institutions and biotech companies, supported by the Marie Skłodowska-Curie Actions, the EURECA represents the first concerted European initiative to harness the epitranscriptome for improving cancer patient care.

**PROSTAMET - "PROSTAMET A Comprehensive Translational Research and Training Pipeline Harnessing Lipid Metabolism to Improve Prostate Cancer Management and Educate Young Researchers in Tackling Complex Disease"** Funding agency: European Commission HORIZON-MSCA-2022-DN-01(Grant agreement ID: 101120283), Budget: 243K€ (2024-2027) [PI@IPO Porto: Prof. Carmen Jerónimo, Coordinator- Prof. Johannes Swinnen (KU Leuven, BE)].

**Description**

In the face of complex multifactorial diseases, such as cancer, and the challenges posed by our aging society, the translation of technological advancements into personalised and cost-effective treatments remains a pressing concern for the scientific community. With the support of the Marie Skłodowska-Curie Actions, the PROSTAMET project will create an immersive Doctoral Network (DN) dedicated to training the next generation of researchers in tackling these types of diseases. With a focus on prostate cancer, the project aims to bridge the gaps in translational research by exploring the untapped potential of altered lipid metabolism. By harnessing a transdisciplinary mindset and education, the project aims to establish a unique lipid-focused research pipeline.

**UCIPredict- "UCIPredict: Circulating tumour microenvironment components as Urothelial Cancer Immunotherapy Response Predictors"** IN COLLABORATION with CIEMAT (Spain)", Funding agency: TRANSCAN-3, ERA-NET: Sustained collaboration of national and regional programmes in cancer research (JTC 2021) co-funded by the European Commission/DG Research and Innovation, Budget: 99K€ (2023-2026) [PI: Prof. Carmen Jerónimo, Coordinator- Dr. Marta Dueñas (CIBER, ES)].

**Description**

UCIPredict will develop an innovative and reliable urine and blood-based biomarker test for response prediction to immunotherapy IT and tumour recurrence, using non-invasive techniques measuring circulating biomarkers from tumour and tumour microenvironment. Implementation of liquid biopsy biomarkers will improve diagnosis, prognosis and prediction of IT response in UC patients. The main objective of this project is to identify molecular and cellular signatures from urine and blood samples to develop a robust and reproducible laboratory tool for personalised therapy and IT response prediction in UC patients. We will 1) Identify potential molecular targets to guide IT treatments in UC, 2) Detect circulating tumour cells (CTCs) and tumour hybrid cells (THCs) in IT treated and metastatic patients and 3) Evaluate immunomodulation for IT outcome.

**CCI4EU "Comprehensive Cancer Infrastructures for the European Union**" Funding agency: 4 EUROPE- HORIZON-MISS-2022-CANCER-01-02-101103746; Budget: 57K€; (2023-2026) [PI@IPO Porto: Prof. Rui Henrique, Coordinators: Carla Finocchiaro, Valentina Lungheu e Maurizio Cicero - Organisation of European Cancer Institutes (OECI-EEIG)]

**Description**

The CCI4EU consortium aims to strengthen the research capacity of Comprehensive Cancer Infrastructures (CCIs) through defining the CCI maturity model; designing customized interventions for the Capacity-Building Program; promoting online courses; implementing specific on-site interventions; and disseminating, exploiting, and reporting results.

**NATIONAL**

**PROMISE- "Multiomic Profiling of Prostate Cancer Extracellular Vesicles to Uncover Molecular Signatures for Biomarker Discovery"**, Funding agency: Fundação para a Ciência e Tecnologia (Technology and Science Foundation) - (2022.04809.PTDC), Budget: 249K€ (2025-2028) (PI: Prof. Carmen Jerónimo).

**Description**

PROMISE is a comprehensive study using leading-edge high-throughput multiomic analysis of extracellular vesicles (EVs) derived from biological samples, encompassing matched tissue and body fluids, obtained from prostate cancer (PCa) patients. This project holds promise for uncovering tumor communication pathways, and most importantly for the identification of EV signatures in liquid biopsies to aid PCa clinical management.

**EpImmunePCa - "On the crossroads of Immuno-Epigenetics for targeting advanced Prostate Cancer"** IN COLLABORATION with INEB/i3S, Funding agency: Fundação para a Ciência e Tecnologia (Technology and Science Foundation) - (2022.04809.PTDC), Budget: 250K€ (2023-2026) (PI: Dr. Margareta Correia, Co-PI-Prof. Rui Henrique).

**Description**

The overall objective of this project is to define a transcriptional and epigenetic profile of cytotoxic tumor-infiltrating lymphocytes, which can be targeted to increase the efficacy of immunotherapies, especially in metastatic castration-resistant prostate

cancer (mCRPC), with the translational aim of combining epi-drug pre-conditioning and adoptive cell transfer targeting PCa tumor-associated molecules.

**Publications:**

Dos Reis FD, Jerónimo C, Correia MP, et al. *Front Immunol.* 14:1152572, 2023. doi: 10.3389/fimmu.2023.1152572.

**PCaEVision- "Decoding the role of extracellular vesicles in prostate cancer bone metastasis"** IN COLLABORATION with Champalimaud Foundation and CNIO (Spain), Funding agency: Fundação para a Ciência e Tecnologia (Technology and Science Foundation) - (2022.05135.PTDC), Budget: 50K€ (2023-2025) (PI: Dr. Vera Constâncio, Co-PI-Dr. Hector Peinado).

**Description**

The overarching aim of PCaEVision is to foster the knowledge of physiopathological processes in PCa bone metastasis development by tackling the contribution of PCa derived extracellular vesicles (EVs) for bone metastasis development in vivo.It is expected that PCaEVision will contribute with: i) the elucidation of the role of EVs produced by PCa primary tumors in bone metastatic disease development, opening a venue for future studies aiming to characterize the molecular alterations caused by PCa derived EVs during bone metastasis initiation and progression, and ii) the identification of new potential biomarkers of PCa aggressive disease. Ultimately these findings could contribute to the improvement of health and survival of PCa cancer patients.

**CONCLUDED**

**MindGaP- "Bridging the gap between Mind, Brain and Body: Exosome role and monitoring"** IN COLLABORATION with UCoimbra, School of Engineering of IPP and European universities (LINU, VTT, and UOULU); Funding agency: H2020-FETOPEN, Budget: 799K€ (2019-2024) (PI: Prof. Rui Henrique; Co-PI: Prof. Carmen Jerónimo). In collaboration with Psychology Service and Breast Clinic

**Description**

MindGAP looks for sensitive health indicators among exosomes that circulate throughout the body and that may change under disease. To this end, the possibility of using MINDFULNESS meditation as a mind-related tool to control the cargo of exosomes is explored. If meditation is successful in changing the behavior and attitudes of many people, it means that the exosomes cargo may be changed through this process. The obtained knowledge aims at opening doors to an innovative device that may be used by everyone to understand his/her health status.

**Publications:**

Monteiro-Reis S, et al. Int J Mol Sci. 22(6):3267, 2021. doi: 10.3390/ijms22063267.
Pedro J, et al. Psychooncology. 30(11):1836-1848, 2021. doi: 10.1002/pon.5771.
Pereira DR, et al. Trials. 23(1):118, 2022. doi: 10.1186/s13063-022-06045-x.

**EpiMarkGermCell – Development of novel prognostic and predictive epigenetic biomarkers for malignant testicular germ cell tumors**; Funding agency: Fundação para a Ciência e Tecnologia (FCT) (POCI-01-0145-FEDER-29043); Budget: 240K€ (2018-2021); (PI: Prof. Dr. Rui Henrique, Co-PI: Prof. Dr. Carmen Jerónimo)

**Description**

The overall objective of the EpiMarkGermCell Project is to discover and validate new epigenetic biomarkers, both prognostic and predictive, for TGCT, thereby enabling improved patient care. Tissue and liquid biopsies will be made available and tested to identify altered patterns of DNA methylation, expression of chromatin-modifying/remodeling enzymes, and miRNA transcription levels. Promising candidate biomarkers will be submitted for European patenting. This project builds on the experience of the Cancer Biology and Epigenetics Group at IPO Porto in developing epigenetic biomarkers for urological cancers.

**Publications:**

Lobo J, et al. Clin Epigenetics, 2021. 13(1): p. 70. DOI: 10.1186/s13148-021-01048-y.
Lobo J, et al. Mol Oncol, 2021. 15(4): p. 846-865. DOI: 10.1002/1878-0261.12909.
Lobo J, et al. Pharmaceutics, 2021. 13(1). DOI: 10.3390/pharmaceutics13010073.
Lobo J, et al. Epigenomics, 2020. 12(18): p. 1579-1592. DOI: 10.2217/epi-2020-0066.
Lobo J, et al. Andrology, 2020. 8(5): p. 1233-1242. DOI: 10.1111/andr.12814.
Fontes-Sousa M, et al. BMCUrol, 2020. 20(1):p.127. DOI:10.1186/s12894-020-00682-7.
Lobo J, et al. Histopathology, 2020. 76(3): p. 486-489. DOI: 10.1111/his.13979.
Lobo J, et al. J Transl Med, 2019. 17(1): p. 79. DOI: 10.1186/s12967-019-1837-z.
Costa AL, et al. Epigenomics, 2018. 10(12): p. 1511-1523. DOI: 10.2217/epi-2018-0034.
Lobo J, et al. Hum Pathol, 2018. 82: p. 113-124. DOI: 10.1016/j.humpath.2018.07.016.
Vilela-Salgueiro B, et al. Philos Trans R Soc Lond B Biol Sci, 2018. 373(1748). DOI: 10.1098/rstb.2017.0338.

**HyTherCaP – Hydralazine: Testing an off-label effect in Castration-Resistant Prostate Cancer**; Funding agency: Fundação para a Ciência e Tecnologia (FCT) (POCI-01-0145-FEDER-29030); Budget: 240K€ (2018-2021); (PI: Prof. Dr. Carmen Jerónimo, Co-PI: Prof. Dr. João F Mano)

**Description**

The overall objective of the HyTherCap Project is to confirm the mechanism of action of hydralazine in CRPC, which possibly involves AR re-expression mediated by demethylation, and to define a predictive biomarker of response to this therapy, enabling the off-label use of hydralazine in a subset of CRPC patients who exhibit AR hypermethylation.

**Publications:**

Antunes J, et al. Acta Biomater, 2019. 94: p. 392-409. DOI: 10.1016/j.actbio.2019.06.012.
Marques-Magalhães Â, et al. Biomed Pharmacother. 141:111681, 2021. DOI: 10.1016/j.biopha.2021.111681.
Pacheco MB, et al. Pharmaceuticals (Basel). 14(7):670, 2021. DOI: 10.3390/ph14070670.
Lopes N, et al. Biomedicines 9(8):976, 2021. DOI: 10.3390/biomedicines9080976.
Moreira-Silva F, et al. Biomed Pharmacother. 150:113031, 2022. DOI: 10.1016/j.biopha.2022.113031.

**TRIMARKCHIP – Assessing the trifecta of cancer circulating biomarkers: a combined microfluidics platform for detection of CTCs, exosomes and ctDNA,** Funding agency: Fundação para a Ciência e Tecnologia (FCT) (POCI-01-0145-FEDER-030831-PTDC/BTM-TEC/30831/2017), Budget: 41K€ (2018-2022) PI@i3S: Prof. Dr. Fernando J Monteiro, Co-PI: Prof. Dr. Carmen Jerónimo

**Description**

The proposed project focuses on the development of an advanced one-chip microfluidic system for the isolation and characterization of three circulating biomarkers found in the peripheral blood of cancer patients: circulating tumor cells (CTCs), circulating tumor DNA (ctDNA), and exosomes. This advanced system will be applied in the diagnosis and prognosis of lung cancer, to support treatment selection and assess cellular response to therapy. Lung cancer remains the deadliest type of cancer worldwide, is difficult to diagnose in its early stages, and is often inaccessible for tumor biopsies. New strategies are needed for the early detection of primary tumors and metastases, as well as for the accurate selection of patient-specific treatments based on tumor mutations. This system would be a powerful and precise tool to evaluate, through a simple blood draw, the complete genetic landscape of the disease—from the primary tumor to potential metastases—enabling continuous, real-time monitoring of each patient's condition.

**Publications:**

Carvalho Â, et al. Biomater Sci. 10(12):3296-3308, 2022. doi: 10.1039/d2bm00044j.

## R&D CONTRACTS WITH PHARMACEUTICAL COMPANIES

**KYMAB-"Immunoprofiling characterisation of clinical samples by IHC and gene expression analysis and correlation with clinical outcomes in support of translational medicine strategies for ICOS and PD-L1-IC antibody therapeutics**." Kymab Ltd. (Cambridge, UK); Budget: 159K€ (2019-2024) (PI: Prof. Dr. Rui Henrique)

**Description**

This project aims to support the application of translational medicine, from initial discovery to clinical development, by strengthening the understanding of target expression in clinically relevant human samples and its correlation with clinical disease characteristics and outcomes.

**Collaborators in Competitive Funded projects:**

- CyclicCell: PTDC/EME-APL/1342/2020
- GLYCOTARGET: PTDC/MEC-ONC/0491/2021
- PRIME-ROSE- Precision Cancer Medicine Repurposing System using pragmatic Trials- HORIZON-RIA- 101104269
- ACCuseD: PTDC/SAU-SER/30388/2017