PROJECTS WITH INTERNAL FUNDING

NanoEpiCirc_mPCa – "Nanoparticle-driven targeting of epigenetic circular RNA networks in metastatic Prostate Cancer" (PI 268-CI-IPOP-50-2026), Budget: 20K€ (2026). (PI: Prof. Carmen Jerónimo)

Description

Prostate cancer (PCa) is one of the leading causes of cancer-related mortality in men, with most patients succumbing to metastatic PCa (mPCa). Although bone metastases are the furthermost common in mPCa, liver metastases are the most lethal. Currently, the mechanisms underlying PCa organotropism remain largely unstudied. Circular RNAs (circRNAs) are covalently closed non-coding RNAs, characterized by their enhanced stability. Increasing evidence suggests that circRNAs can regulate key processes, including cell proliferation, invasion, and epithelial-mesenchymal transition, partly through interactions with epigenetic enzymes, which remain largely unexplored. Therefore, we aim to elucidate the mechanisms connecting circRNAs and epigenetic enzymes in mPCa, and uncover how their interplay may influence organotropism, ultimately developing strategies to detect and prevent these processes.

ImpReSario – "Implementation of the RAD51-FFPE test as a biomarker for HRD in ovarian high-grade serous carcinoma" (PI236-CI-IPOP-33-2025), Budget: 10K€ (2025-2026) (PI: Dr Carla Bartosch)

Description

High-grade serous ovarian carcinoma (HGSOC) is the most lethal type of gynecological cancer and carries a poor prognosis due to late diagnosis and treatment resistance. Around 50% of HGSOC cases exhibit homologous recombination deficiency (HRD), often caused by alterations in the BRCA1/2 genes or other homologous recombination repair (HRR) genes. Detecting HRD is essential for guiding therapies such as PARP inhibitors and bevacizumab. However, current methods—such as genetic sequencing and the analysis of "genomic scars"—have limitations, as they do not reflect the tumor's current DNA repair status. The ImpReSario project aims to standardize the RAD51-FFPE test—a functional assay that evaluates RAD51 protein accumulation in paraffin-embedded tumor samples, allowing real-time assessment of HRD. The project also aims to correlate test results with genomic and clinical data, improving diagnostic accuracy and promoting personalized therapeutic strategies for HGSOC.

DEBILItAte – "Dissecting histopathological and epigenetic biomarkers of intraductal, indolent and aggressive prostate carcinomas" (PI239-CI-IPOP-35-2025), Budget: 20K€ (2025-2026) (PI: Prof. João Lobo)

Description

The goal of the DEBILItAte project is to address the key challenges of prostate cancer (PCa) by following the patient journey from early stages to advanced and metastatic disease, including castration resistance. To achieve this, the project aims to identify and validate histopathological and epigenetic features with prognostic value and clinical utility. This includes studying the role of epithelial-mesenchymal transition in these tumors, determining DNA methylation patterns, histone expression, and evaluating differential miRNA levels across different PCa phenotypes—such as

intraductal carcinoma, cribriform prostate cancer, and tumors with neuroendocrine transdifferentiation. To meet these objectives, technologies such as image analysis and array-based methodologies will be used to discover relevant biomarkers. The expected outcome is the validation of biomarkers that improve patient outcomes, translating laboratory findings into real clinical benefit.

Screen4Cancer – "A Prospective Multicentric Study Evaluating a Novel DNA Methylation Blood Test for Multi-Cancer Early Detection" (PI243-CI-IPOP-38-2025), Budget: 20K€ (2025-2026) (PI: Prof. Rui Henrique)

Description

Cancer remains one of the greatest global public health challenges, with over 20 million new cases and 9.7 million deaths recorded in 2022. The four most common cancer types—lung, breast, colorectal, and prostate—account for a significant share of this burden. Current screening methods for these cancers have major limitations, such as invasiveness, radiation exposure, and high false-positive rates, highlighting the urgent need for more effective and less invasive detection strategies. Our team has developed an innovative blood-based test for multi-cancer early detection (MCED) through the analysis of circulating cell-free DNA (cfDNA) methylation. This test, based on digital PCR (ddPCR) technology, is cost-effective, minimally invasive, and capable of detecting multiple cancer types simultaneously. Following promising results, the PanCancer project proposes a prospective multicenter clinical study in Portugal to validate the test's effectiveness in real-world settings, aiming to improve early detection and patient outcomes.

SuHRBlaC – "Surveillance of patients with high-risk non-muscle invasive bladder cancer: validation of a DNA methylation-based test in a real-world setting" (PI239-CI-IPOP-35-2025), Budget: 10K€ (2025-2026) (PI: Dr. João André Carvalho)

Description

Bladder cancer (BC) is the tenth most frequently diagnosed cancer worldwide. In the follow-up of non-muscle invasive bladder cancer (NMIBC), the current standard includes cystoscopy (CYSTO), an invasive procedure, and urine cytology, which has limitations in sensitivity and reproducibility. To reduce the morbidity, discomfort, and costs associated with CYSTO, this project proposes to evaluate the clinical performance and cost-effectiveness of Bladder EpiCheck™, a non-invasive urine test based on the methylation of 15 DNA sequences associated with BC. The study aims to validate a cutoff value (EpiScore) to enable early detection of recurrences and progression in patients with high-grade NMIBC (pT1 and pTis), as well as to compare its effectiveness with urine cytology. The test's specificity against other urological neoplasms and urinary infections will also be assessed. Its implementation could represent a significant advancement in personalized and less invasive monitoring of bladder cancer.

EpiLungScreen – "Epimarkers for Lung Cancer Screening in Liquid Biopsies" (PI248-CI-IPOP-29-2025), Budget: 10.6K€ (2025-2026) (PI: Prof. Carmen Jerónimo; Prof. Rui Henrique)

Description

Lung cancer is the leading cause of cancer-related death worldwide, often diagnosed at advanced stages due to the lack of effective and accessible screening methods. Although low-dose computed tomography (LDCT) has shown some effectiveness in

early detection, its technical and economic limitations prevent its widespread adoption as a screening tool. In this context, the EpiLungScreen project aims to identify and validate a gene methylation panel with potential use as a biomarker in liquid biopsies—a promising, non-invasive approach based on the analysis of circulating cell-free DNA (ccfDNA). The detection of specific epigenetic alterations, such as DNA methylation patterns, could enable the early diagnosis of lung cancer, helping to reduce the mortality associated with this disease.

EMBRACIVE – "A microfluidic assisted technology for non-invasive identification and characterization of extracellular vesicles in bladder cancer patients" (PI224-CI-IPOP-74-2024), Budget: 15K€ (2024-2026) (PI: Prof. Carmen Jerónimo)

Description

Bladder cancer is a highly prevalent disease with significant clinical and economic impact. Although most cases correspond to non-muscle invasive bladder tumors (NMIBC), more than half progress to invasive forms (MIBC), which are associated with poor prognosis and high mortality. Continuous surveillance is essential due to the high recurrence rate, but it relies on invasive and costly methods such as cystoscopy. At the same time, currently available urinary tests have limited sensitivity and specificity and are not widely recommended in clinical guidelines. In this context, the present project aims to characterize the origin of extracellular vesicles (EVs) associated with bladder cancer, using both tissue samples and liquid biopsies from affected patients. By identifying specific molecular biomarkers present in EVs, the project seeks to contribute to the development of more accurate, non-invasive methods for the diagnosis, monitoring, and risk stratification of bladder cancer patients.

MethyProCancer – "Prostate Cancer Risk Stratification and monitoring approach: Unveiling circulating DNA methylation-based biomarkers" (PI189-CI-IPOP-22-2023), Budget: 25K€ (2023-2026) (PI: Prof. Carmen Jerónimo; Co-PI Prof. Rui Henrique)

Description

Although most prostate cancers (PCa) are not life-threatening, around 20% of cases are aggressive and are linked to poor prognoses. PSA-based screening led to death rates decreased, but overdiagnosis and consequent overtreatment has considerably increased. Hence, it is urgently necessary to develop more effective techniques that would enable reliable categorization of unfavorable intermediate-risk (uirPCa) and high-risk PCa (hrPCa), as well as to monitor quantifiable residual disease after therapy.

Early PCa events involving altered DNA methylation are easily detected in liquid biopsies and are useful for reliable diagnostic, prognostic, and response prediction tools. Herein, we aim to explore minimally invasive DNA methylation-based biomarkers suited for stratification of uirPCa and hrPCa as well as residual disease surveillance, unveiling a potential improvement in the PSA-based screening.

Publications:

Sequeira JP, et al. Cancers (Basel). 16(7):1363, 2024. doi: 10.3390/cancers16071363.

miREpiTestis – "Unveiling miR-371-373 cluster epigenetic reprogramming and downstream targets in testicular germ cell tumors" (PI190-CI-IPOP-23-2023), Budget: 35K€ (2023-2026) (PI: Prof. Carmen Jerónimo; Co-PI Dr. João Lobo)

Description

To date, miR-371a-3p is the most promising tumor marker of testicular germ cell tumors (TGCTs) and is expected to enter the clinic soon due to its high sensitivity and specificity. Despite undoubtful clinical utility, little is known about miR-371a-3p biology, secretion and regulatory networks. Hence, the miREpiTestis project aims to 1) uncover miR-371-373 (upstream) epigenetic regulatory mechanisms, 2) determine miR-371a-3p stemness-related (downstream) target genes, and 3) ascertain its secretion in TGCT-derived extracellular vesicles.

Publications:

Tavares NT, Lourenço C, Constâncio V, et al. Cell Commun Signal. 23(1):252, 2025. doi: 10.1186/s12964-025-02250-8.
Lobo J, Tavares NT, Fonseca D, et al. J Pathol. 266(2):160–176, 2025. doi: 10.1002/path.6412.
Cantante M, Miranda-Gonçalves V, Tavares NT, et al. Andrology. Published online ahead of print, 2024. doi: 10.1111/andr.13824.
Lobo J, et al. Hum Pathol, 48:66-71, 2024. DOI: 10.1016/j.humpath.2024.05.005
Estevão-Pereira H, et al. Andrology. 2024. DOI: 10.1111/andr.13604.
Tavares NT, et al. Curr Opin Urol, 34(1):20-26, 2024. DOI: 10.1097/MOU.0000000000001137

EpiPaRTy - "Advances in Epigenetic targeting for PCa: Dissecting the interplay between ncRNAs and chromatin remodelers and their role as biomarkers of RadioTherapy resistance" (PI-159-CI-IPOP-152-2022), Budget: 55K€ (2021-2026) (PI: Prof. Carmen Jerónimo).

Description

Despite the high survival rates, some prostate cancer (PCa) tumors acquire an aggressive phenotype and might disseminate, becoming resistant to therapy, as the external beam radiation therapy, which is proven to have decreased effectiveness in more advanced stages, with the appearance of biochemical recurrences or metastization. According to cell death challenge in radiation-based therapy, epigenetic alterations, including non-coding RNAs and chromatin remodelling modifications deregulation, affect the expression of several critical target genes related to the cell growth, DNA damage repair and cell cycle deregulation. Thus, herein we aim to discover novelty therapeutic strategies against major epigenetic players that might reverse radioresistant PCa phenotype, as well as, unveiling novel prognostic and predictive biomarkers with a clinical value in PCa patient stratification.

Publications:

Macedo-Silva C, Albuquerque-Castro Â, Carriço I, et al. Cell Death Discov. 11(1):306, 2025. doi: 10.1038/s41420-025-02597-4.
Macedo-Silva C, et al. Signal Transduct Target Ther. 8(1):395, 2023. doi: 10.1038/s41392-023-01639-6.
Macedo-Silva C, et al. Clin Epigenetics. 13(1):125, 2021. doi: 10.1186/s13148-021-01111-8.

MiRVeBlad- "Identification of Exosomal-derived miRNAs as non-invasive high-risk BlCa biomarkers" (PI-160-CI-IPOP-153-2021), Budget: 55K€ (2021-2026). (PI: Prof. Carmen Jerónimo, Prof. Rui Henrique) This project has been developed within the frame of Porto.CCC

Description

Extracellular vesicles (EVs) have an essential functional role in local tumor progression, metastatic spread, and emergence of drug resistance in different types of cancer. As such, EVs are being explored as potential diagnostic, prognostic, and predictive markers of malignancy. Virtually all biomolecules (such as DNA, RNA, ncRNA or proteins) present within EVs can be tested. In the setting of urothelial tumors, there is recent evidence suggesting that EVs reflect the molecular signature of the primary tumor cells and can, therefore, serve as an effective tool for molecular characterization of tumors themselves as well as to uncover clinical useful biomarkers We aim to discover and validate these biomarkers in liquid biopsies from patients with urothelial tumors. Effective biomarkers will allow us to diagnose tumors at early stages and to adequately stratify low- and high-risk lesions.

Publications:

Teixeira-Marques A, et al. Sci Rep. 2024 May 28;14(1):12267. DOI: 10.1038/s41598-024-62783-9.
Teixeira-Marques A, et al. Int J Mol Sci. 24(7):6757, 2023. DOI: 10.3390/ijms24076757.
Montezuma D, et al. Epigenomics. 13(19):1514-1521, 2021. DOI: 10.2217/epi-2021-0333.

PCaEXOBone - "Prostate Cancer pre-metastatic niche formation: Exosomal osteotropism" (PI 158-CI-IPOP-151-2021), Budget: 70K€ (2021-2026). (PI: Prof. Carmen Jerónimo)

Description

Prostate cancer (PCa) is a major public health concern worldwide. Despite the high incidence, PCa-related deaths are mostly due to metastatic disease, for which no curative treatments are available. Although bone metastasis represents up to 84% of all PCa metastasis, the mechanisms underlying PCa osteotropism remain largely unknown.
Exosomes can transfer their cargo, functionally impacting recipient cells. Thus, exosomes have been linked with the formation of pre-metastatic niches by creating a distant pro-tumour environment. Moreover, although exosomes have been associated with metastatic organ tropism in several cancer types, exosomal signatures and their biological relevance in PCa carcinogenesis and metastization are still poorly understood. Therefore, we aim to unravel the function of PCa derived exosomes in bone metastasis development and identify exosomal cargo contributing to osteotropism. Additionally, we intend to develop a specific prognostic tool of bone pre-metastatic niche formation able to predict the likelihood of progression to metastatic disease.

PlatiMethylPredict – "Promoter methylation of DNA repair genes as biomarker of response to platin-based chemotherapy" (PI247-CI-IPOP-162-2021), Budget: 15K€ (2021-2026) (PI: Prof. Carmen Jerónimo; Prof. Rui Henrique)

Description

The PlatiMethylPredict project aims to identify methylation changes in the promoters of genes involved in DNA repair that could serve as predictive markers of chemotherapy response in patients with bladder carcinomas. Using a combined approach of *in silico* analysis and clinical validation in tissue samples and liquid biopsies, the project seeks to characterise the relationship between methylation and treatment response, to optimise patient selection and personalise therapeutic protocols. This project will contribute to the identification of biomarkers capable of

predicting resistance and improving the effectiveness of chemotherapy in these patients.

Publications:

Tavares NT, Gumauskaitė S, Lobo J, et al. Cancers (Basel). 14(12):2918, 2022. doi: 10.3390/cancers14122918.

DNAmeCERVIX- "DNA methylation biomarkers for triage of hrHPV positive cases in the Northern Portugal population-based cervical cancer screening program" funded by the Research Centre of Portuguese Oncology Institute (PI 142-CI-IPOP-130-2020), Budget: 45K€ (2020-2026) (PI: Prof. Carmen Jerónimo; Co-PI: Prof. Rui Henrique). In collaboration with ARS-Norte.

Description

HPV-based screening strategies attain high throughput due to automation and display high sensitivity, compared to cytology, but they lack specificity, especially among young women, due to the high prevalence of transient infections. Nonetheless, DNA methylation has shown promise as a triage marker for referral to colposcopy of HR-HPV-positive women, disclosing higher sensitivity than cytology in this setting. The main aim of this project is to validate a panel of DNA methylation-based markers as a triage test for women with HR-HPV positive testing in the context of population-based cervical cancer screening.

Publications:

Salta S, Sequeira JP, Amorim-Fernandes B, et al. MedComm (2020). 6(7): e70203, 2025. DOI: 10.1002/mco2.70203.
Salta S, et al. J Infect Public Health, 17(6):1057-1064, 2024. DOI: 10.1016/j.jiph.2024.04.020
Salta S, et al. Clin Epigenetics, 15: 125, 2023. DOI: 10.1186/s13148-023-01537-2
Salta S, et al. Int J Cancer, 149(11):1916-1925, 2021. DOI: 10.1002/ijc.33778.

DECODE-PCa - "Epigenetic regulation of non-coding RNAs in Prostate Cancer" (PI 157-CI-IPOP-121-2019), Budget: 45K€ (2021-2026). (PI: Prof. Carmen Jerónimo)

Description

Decoding PCa aims to provide further insights into basic medicine and how non-coding RNA chemical alterations can be translated into the clinical practice. The specific regulatory mechanisms through which epitrancriptomics can inhibit or promote cancer onset and progression depends essential on 2 aspects: (1) whether the chemical modifications target oncogenes or tumor suppressor RNAs; (2) changes in the expression or activity of the molecules responsible for install/remove the modifications. Therefore, clarifying epitranscriptomic target genes and related pathways is mandatory to understand the mechanistic impact of RNA modifications in cancer biology. We aim to tackle whether unveiled RNA methylation profiles may be helpful to clarify the mechanisms behind prostate cancer and to improve clinical decisions and existing therapies.

Publications:

Barros-Silva D, et al. Biotechniques. 74(5):225-235, 2023. DOI: 10.2144/btn-2022-0122.
Barros-Silva D, et al. Cancers 12(4): E771, 2020. DOI: 10.3390/cancers12040771.