UCD DUBLIN

THE MATER HOSPITAL

CANCER RESEARCH SYMPOSIUM

15 September 2023

2PM

Catherine McAuley Centre
The Mater Hospital

AGENDA

13:30	***Registration & Refreshments***	
14:00 - 15:00	**Session 1: Welcome & Site Updates**	
14:00	**Welcome** *Session open and welcome*	**Dr Anne Fortune** *Consultant Haematologist, Mater Misericordiae University Hospital*
14:05	**Mater Misericordiae University Hospital Update** *Update on cancer research at MMUH and the Clinical Trial Research Unit*	**Dr Anne Fortune** *Consultant Haematologist, Mater Misericordiae University Hospital*
14:10	**St Vincent's University Hospital Update** *Update on cancer research at SVUH and the Cancer Clinical Research Trust*	**Dr Mark Doherty** *Consultant Medical Oncologist, St Vincent's University Hospital*
14:15	**University College Dublin Update** *Update on UCD schools and affiliated cancer research clusters*	**Professor Bill Watson** *Professor of Cancer Biology, UCD School of Medicine*
14:20	**UCD Cancer Trials Cluster Update** *Update on accrual and activity of the UCD Cancer Trials Cluster*	**Professor Michaela Higgins** *Consultant Medical Oncologist, St Vincent's University Hospital*
14:25	**National Cancer Mission Hub** *Overview of the Irish contingent of the EU project, 'ECHoS' - Establishing of Cancer Mission Hubs: Networks and Synergies.*	**Prof Liam Gallagher** *Professor of Cancer Biology, UCD*
14:35	**START Centre Update** *An update on the new early phase clinical trial centre located at the Mater Hospital.*	**Dr Austin Duffy** *Consultant Oncologist, Mater Misericordiae University Hospital*
14.45	**Returning Clinicians Update** *Clinicians returning from the Memorial Sloan Kettering Cancer Center will discuss their work in:* • *Novel Technologies and Lynch Syndrome &* • *ctDNA in gastrointestinal malignancies*	**Drs Darren Cowzer &** **Emily Harrold** *Consultant Medical Oncologists, Mater Misericordiae University Hospital.*
15:00 - 15:30	**Session 2: Panel Discussion**	

"Developing Research Partnerships and Closing the Academic-Clinical Gap"

Prof Ronan Cahill (*Professor of Surgery*), Prof Patricia Fitzpatrick (*Professor of Epidemiology & Biomedical Statistics*), Dr Barry Kevane (*Consultant Haematologist*), Dr Sinead Lynch (*Senior Counselling Psychologist*), & Prof Amanda McCann (*Professor, UCD School of Medicine*). Facilitator: Dr Geraldine O'Sullivan Coyne (*Consultant Oncologist*),

15:30	**Networking break and poster viewing (refreshments provided)**

16:00 - 17:00	**Session 3: Clinical-Academic Research Partnerships**	
16:00	The FEED Study (a Fish oil supplement, pancreatic Enzyme supplement, Exercise advice and individualized Dietary counselling)	**Dr Oonagh Griffin** *St Vincent's University Hospital*
16:10	Dyadic Psychoeducational Interventions for people with Advanced cancer and their Informal Caregivers (DIAdIC)	**Professor Suzanne Guerin & Aoife McCann** *UCD School of Psychology*
16:20	The Sleepio After Cancer Study – Digital CBT for insomnia in women cancer patients. A demonstration of the collaborative efforts between clinicians and academics.	**Dr Teresa Tracey** *Living Well Cancer Programme & UCD School of Medicine*
16:30	Answers for Cancers: Nurse-led cancer support for patients.	**Anne-Marie Fay & Michelle Matthews** *Mater Misericordiae University Hospital*
16:40	Exploring Hypercoagulability in Myeloproliferative Neoplasms: The EMPRESS Study	**Dr Sarah Kelliher** *ICAT Fellow, Mater Misericordiae University Hospital*
16:50	The COMFORT trial: a randomised control trial comparing group-based COMpassion-FOcussed therapy and breathing pattern ReTraining with treatment as usual on the psychological functioning of patients diagnosed with cancer recurrence during COVID.	**Dr Sinead Lynch** *Senior Counselling Psychologist, Psycho-Oncology, Mater Misericordiae University Hospital*
17:00	Meeting Close	**Dr Anne Fortune** *Consultant Haematologist, MMUH*

17:00 - Art Exhibition and Wine Reception

Following the symposiuum, we invite attendees to stay for a wine reception and special presentation art exhibition with artists, **Vincent Devine** and **Navin Hyder**.

Vincent Devine's work, *The Vitruvian*, is a bespoke piece of artwork, which explores the labyrinth world of cancer research through visual media. This work was created in collaboration with cancer researchers in UCD.

Navin Hyder is the Artist-in-Residence at the Mater Hospital, whose work includes the '*Memento Vivere: A Series of Works Made at the Mater Hospital, Dublin'*

POSTER ABSTRACTS

1	Despina Bazou	Proteomic Characterisation of BMNCs and Blood Plasma in Extramedullary Multiple Myeloma Identifies Potential Prognostic Biomarkers
2	Caoimbhe Burke	Multiplex In Situ Hybridisation for the Detection and Visualisation of OncoMasTR Target Gene Expression in Breast Cancer Tissue
3	Helen Goodman	Cancer Clinical Trial Nurse Preceptorship Award
4	Chowdhury Arif Jahangir	Exploration of the Interplay between Master Transcriptional Regulators and Immune Cells within the Tumour Microenvironment of Breast Cancer
5	Bindu Krishnanivas	“Smart Selection” Automating Clinical Trial Recruitment Steps
6	Beatriz Pinheiro Lopes	Cold plasma deposition as a novel technology for targeted cancer drug delivery
7	Michelle Matthews	Exploring the role of an enhanced patient information leaflet in patient participation and understanding of terminology in cancer clinical trials.
8	Clodagh Murphy	Investigating the Therapeutic and Prognostic Utility of Long Non-Coding RNA Targets and their Association with Tumour Microenvironment in KRAS-Mutant NSCLC.
9	Carla O'Neill	Family-Centred Cancer Care End of Life Education (FCCC-EoLEd)

Posters will be presented in the symposium lobby at 3.30PM

Abstracts

1 Proteomic Characterisation of BMNCs and Blood Plasma in Extramedullary Multiple Myeloma Identifies Potential Prognostic Biomarkers

D. Bazou* [1, 2], K. Dunphy [3], P. Dowling [3]. & P. O'Gorman [2]

1. *School of Medicine, University College Dublin.*
2. *Department of Hematology, MMUH, Dublin.*
3. *National University of Ireland: Maynooth, Maynooth*

Extramedullary Multiple Myeloma (EMM) is characterised by the ability of myeloma cells to grow independently of the bone marrow microenvironment and colonise extramedullary sites. EMM is associated with poor prognosis and drug resistance. Studies on the molecular mechanisms of EMM are limited. We performed a label-free mass spectrometry (MS) analysis of bone marrow mononuclear cells (BMNCs) and blood plasma from MM patients with and without EMM to improve our understanding of EMM pathogenesis.

MS analysis of matched medullary MM (n=8) and EMM (n=9) BMNCs and blood plasma samples was performed. Plasma proteins selected for verification were analysed by enzyme linked immunosorbent assay (ELISA). Receiver operating characteristic (ROC) curve analysis determined the diagnostic potential of the proteins.

We identified distinct proteomic profiles of EMM and MM BMNCs. Proteins increased in EMM BMNCs were associated with cell adhesion and migration, whereas those decreased in abundance were associated with metabolic pathways, e.g. tricarboxylic acid cycle. Vascular cell adhesion molecule 1 (VCAM1), hepatocyte growth factor activator (HGFA), and pigment epithelium-derived factor (PEDF) were significantly increased in EMM patient plasma, demonstrating high discriminatory power for EMM diagnosis.
Our study provides further insight into the molecular mechanisms within EMM and holds potential to provide a more personalised therapeutic approach for EMM patients.

2 Multiplex In Situ Hybridisation for the Detection and Visualisation of OncoMasTR Target Gene Expression in Breast Cancer Tissue

Caoimbhe Burke* [1], Chowdhury Jahangir [1], Joseph McGinley [1], Claudia Aura [1], Grace Gormley [1], Clodagh Murphy [1], Christine McCaffrey [1], Fiona Lanigan [1], Adrian Bracken [2], Björn Nodin [3], Karin Jirström [3], Arman Rahman [1], and William M. Gallagher [1]

1. *UCD School of Biomolecular & Biomedical Science, UCD Conway Institute*
2. *Smurfit Institute of Genetics, Trinity College Dublin Department of Clinical Sciences, Division of Oncology and Pathology, Lund University, Lund, Sweden*
3. *Division of Oncology and Pathology, Lund University, Lund, Sweden*

Previously, we have identified a novel prognostic gene panel named OncoMasTR, comprising of a set of master transcriptional regulators (MTRs), which when assessed with RT-qPCR outperformed other commercial prognostic signatures in successfully stratifying early-stage breast cancer patients into high and low risk categories for distant recurrence. Most RT-qPCR based assays do not relay the spatial context of gene expression, as samples are homogenised prior to running the assay. Moreover, due to variations in quality of antibody reagents, ensuring specificity and reproducibility is always a concern in protein-based immunohistochemistry assays.

RNA in situ hybridisation (ISH) can offer digital pathology-based quantification of gene expression within histological samples, while displaying spatial distribution of the RNA transcripts which may also carry important prognostic information. We have used the RNAscopeV2 assay to successfully detect the OncoMasTR target gene, UHRF1, in a breast cancer tissue microarray (TMA) cohort (n = 498). UHRF1 mRNA expression as determined by ISH showed moderate correlation with protein expression measured by IHC (R = 0.55, p < 2.2e-16) and mRNA expression of bulk tissues quantified by RT-qPCR (R = 0.23, p = 0.0015). Survival analysis with the single plex data showed high expression of UHRF1 was associated with reduced distant recurrence-free survival (HR = 2.03, p = 0.001), aligning with IHC and RT-qPCR data. We have established a duplex ISH staining and image analysis workflow combining UHRF1 and ZNF367, which has been validated on cell line and full face tissue with TMA staining also complete. Preliminary analysis again suggests that high UHRF1 expression is associated with reduced distant recurrence-free survival, however analysis of data generated from both markers is still ongoing.

3 Cancer Clinical Trial Nurse Preceptorship Award

Helen Goodman*

Cancer Clinical Research Trust, St Vincent's University Hosptial

Background:
Last year, the Irish Cancer Society launched the Cancer Clinical Trial Nurse Preceptorship Award with the aim to encourage more nurses to pursue a career in cancer trials and in doing so, increase awareness of the value of cancer clinical trials. I was selected as an awardee and afforded the opportunity to complete an observership in the Princess Margaret Hospital (PMH) in Toronto, Canada. The Princess Margaret Hospital is the largest cancer centre in Canada and one of the top 5 cancer centres worldwide.

Objectives:
The focus of my experience was to develop a long-lasting synergistic relationship with a world leading centre, review the role of Public

and Patient Involvement within PMH, enhance my own career development and explore the role of an advanced nurse practitioner in oncology research.

Evaluation and Implementation:
My poster presentation will evaluate the contrasts between the PMH research centre and the research unit within the Cancer Clinical Research Trust. My experience highlighted the differences in accessibility of clinical trials for oncology patients within Ontario in comparison to Ireland by using tools such as online platforms for patients to self-refer for clinical trials and availing of a specialised advanced nurse practitioner responsible for onboarding phase 1 patients.

I observed the methodical organisational structure of their vast research program by shadowing their nursing, medical and administrative research staff.

As a result, I will outline how we have made changes to improve our unit's efficiency by progress mapping and expanding the usage of IT in our roles.

4 Exploration of the Interplay between Master Transcriptional Regulators and Immune Cells within the Tumour Microenvironment of Breast Cancer

Chowdhury Jahangir* [1], Claudia Aura [1], Caoimbhe Burke [1], Clodagh Murphy [1], Amir Jalali [2], Fiona Lanigan [1], Adrian Bracken [3], Björn Nodin [4], Karin Jirström [4], Arman Rahman [1], and William M. Gallagher [1, 5]

1. *UCD School of Biomolecular and Biomedical Science, UCD Conway Institute, University College Dublin*
2. *School Of Medicine, National University of Ireland, Galway*
3. *Smurfit Institute of Genetics, Trinity College Dublin*
4. *Division of Oncology and Pathology, Lund University, Lund, Sweden*

We previously identified OncoMasTR, a novel prognostic gene panel of master transcriptional regulators that predicted recurrence risk for lymph node-negative breast cancer (BC) patients better than current prognostic signatures when assessed at an mRNA level. Given the established prognostic utility of immune markers in BC, we hypothesise that integrating immune status information will improve the prognostic power of OncoMasTR. In this study, we evaluated the prognostic potential of the OncoMasTR panel and selected immune populations (T cell, B cell, and macrophage) at the protein level in the context of early-stage breast cancer.

We examined nine OncoMasTR biomarkers through chromogenic immunohistochemistry individually and profiled five immune markers (CD8, CD4, FOXP3, CD20, CD68) using multiplex immunofluorescence (mIF) in a breast cancer tissue microarray cohort (n = 498). Prognostic efficacy of the markers was assessed using univariate and multivariate modeling. An optimal three-marker signature was identified, which when combined with clinical markers (tumour size, nodal involvement, tumour grade), demonstrated enhanced prognostic efficacy (concordance-index = 0.810; likelihood-ratio = 48.985) in comparison to another model containing exclusively OncoMasTR and clinical markers. Out of the immune markers analysed, high entire core (HR = 2.13, p = 0.01) and stromal (HR = 1.8, p = 0.01) macrophage infiltration were significantly associated with worse distant metastasis-free (DMFS) survival. When the spatial architecture of the markers were explored, closer proximity of cytotoxic T cells (CD+) to the tumour cells (PanCK+) was found to be correlated with better DMFS outcomes. Efforts are underway to develop a mIF panel comprising both OncoMasTR and immune markers, potentially offering better prognostic prediction for early-stage breast cancer than current approaches alone.

5 "Smart Selection" Automating Clinical Trial Recruitment Steps

Bindu Krishnanivas*, Lisa Berkley, Maria Meehan, Jane Culligan, Gráinne Cunniffe

Mater Misericordiae University Hospital

Our aim is to maximise cancer trial access and outcomes to prolong patient lives and expand cancer research in Ireland. In order to identify suitable/eligible candidate for available clinical trial is labour intensive process.

Background: Selecting patients from clinic lists (300/week) who may be eligible for ongoing cancer clinical trials is a lengthy, laborious, and inefficient process, currently wasting valuable nursing hours. The patients, hospital and sponsors all benefit from maximizing patient recruitment. Eligibility is defined by the inclusion and exclusion criteria for specific open trials. Demographics and clinical data comprise a significant portion of these criteria, information which must be manually retrieved from various sources (e.g. patient charts, GP letters) by the trials team. Lean-six sigma tools and methodologies enabled process mapping, and three separate solutions were identified and implemented to remove wasteful steps.

Methodology: Lean Six Sigma Findings/Results: The first solution targeted the initial process map step, determining that introducing a "clinical register identifier" function on patient centre removed the necessity to review a separate excel sheet register. Implementing a "patient screening record" document on patient centre ensured the same patient is not screened multiple times when they return to clinic, removing an additional 4 process map steps. Ultimately, a bespoke database, first-of-its-kind, containing most of the required eligibility criteria information is currently being rolled out, identifying eligible patients based on available data, and providing a candidate list for final screening, suitable for use across all clinical trials.

6 Cold plasma deposition as a novel technology for targeted cancer drug delivery

Beatriz Pinheiro Lopes*

School of Chemical and Bioprocess Engineering, University College Dublin

Glioblastoma multiforme (GBM) is the most common, malignant and aggressive brain cancer. Despite many innovations regarding GBM treatment, the final outcome is still very poor, making it neces-

-ssary to develop new therapeutically approaches. Cold Atmospheric Plasma (CAP) as well as Plasma-Activated Liquids (PAL) are being studied as new possible approaches against cancer, based on the detrimental effects of plasma-reactive species such as reactive oxygen and nitrogen species (RONS) on multiple cellular targets which lead to cell death.

The overall research aim is to explore the therapeutic properties of a combination between plasma based technologies and Topotecan (TPT), an antineoplastic agent with major cytotoxic effects during S-phase of the cell cycle, on a human brain cancer cell line (U-251mg).

Combined treatments with plasma-activated water (PAW) and TPT showed a reduction of the metabolic activity and cell mass, an increase of apoptotic cell death, and a reduction of the long term survival. Single applications of PAW+TPT treatments were able to inhibit cell growth as well as cell survival of glioblastoma cells, showing a cytotoxic effect in short term and an anti-proliferative effect in long term.

Plasma has also been demonstrated to efficiently deposit pharmaceuticals onto living tissue and could present a novel method for cancer drug delivery. Evaluation of the plasma-based TPT deposition onto cells could reveal new avenues for more efficacious treatment methods with lower side effects, for application in margin treatment after tumour resection.

7 Exploring the role of an enhanced patient information leaflet in patient participation and understanding of terminology in cancer clinical trials.

Michelle Matthews*

Clinical Trial Research Unit, Mater Misericordiae University Hospital

The National Cancer Strategy 2017–2026 has set ambitious goals over the course of the strategy aimed at increasing patient participation in cancer clinical trials in Ireland. The strategy has called out the importance of cancer clinical trials as an integral and fundamental aspect of national cancer centres. Their aim is to increase the percentage of patients on cancer therapeutic clinical trials to 6%. In order to help with meeting this goal it is essential to ensure that the target patient population and their educational needs are at the forefront of the care we deliver.

The current process for educating and recruiting patients for cancer clinical trials is providing patients with a patient information leaflet (PIL) about the purposed clinical trial that has been prepared by the study sponsor and includes information regulated by governing bodies such as the National Research Ethics Committee (NREC) and Health Product Regulatory Authority (HPRA).

The information within a PIL can be complex and difficult to understand and considering a lot of the clinical trial terminology is new for the patient we have a responsibility to ensure that patients being approached about clinical trial participation are educated in a language they can understand. Unfortunately as it currently stands O' Sullivan et al (2020) demonstrated that patients need a minimum of third level education to understand the information in these PILs. The purpose of this research proposal is to understand if the addition of an enhance PIL in the form of an audio-visual booklet accompanying the current PIL increases patient participation in clinical trials and increases their knowledge and understanding of the trial and the trial procedures.

8 Investigating the Therapeutic and Prognostic Utility of Long Non-Coding RNA Targets and their Association with Tumour Microenvironment in KRAS-Mutant NSCLC.

Clodagh Murphy*, Prof. Arman Rahman, Caoimbhe Burke, Chowdhury Arif Jahangir, Prof. Aurelie Fabre, Dr. Deirdre Kelly, Dr. Calvin Flynn, Prof. Rory Johnson, Prof. William Gallagher.

Cancer Biology and Therapeutics lab & GOLD Lab, UCD.

Lung cancer is the leading cause of cancer-related mortality. 85% of cases are classified as non-small cell lung cancer (NSCLC), with 40% of these bearing an oncogenic KRAS mutation. Despite its prevalence, mutated KRAS remains associated with poor prognosis(1). There is a need for a novel therapeutic and prognostic biomarker panel for KRAS-mutated NSCLC. The work of research teams in UCD sets the foundation for the identification of such a panel.

Professor Johnson (Project co-supervisor) has identified 80 candidate lncRNA therapeutic targets for KRAS-mutant NSCLC via CRISPR cell-line screens and antisense-oligonucleotide (ASO)-based screens in 2D/3D models (2). lncRNAs, while implicated in cancer-specific tumorigenesis, drug-resistance and metastasis, remain largely uncharacterised, highlighting an extremely fruitful research opportunity (3,4). The first aim of the project is continued elucidation of lncRNA targets from this workflow. The second aim is to analyse target prevalence in a cohort of representative patient tissue samples using qRT-PCR and in-situ hybridisation. On identification of prevalent targets, a third aim is to confirm therapeutic efficacy of targets utilising ASO-based investigation in patient explants.

Regarding prognostic biomarker panel development, Professor Gallagher (Project supervisor) has an established pipeline for the identification and validation of multi-marker panels, having co-founded OncoMark which developed OncoMasTR, a CE-marked prognostic test for early-stage breast cancer (5). A fourth aim is to investigate the prognostic potential of lncRNA targets, via expression analysis within a retrospective TMA cohort.

The relationship between the tumour microenvironment and immune markers has prognostic utility in KRAS-mutant NSCLC (1). The Gallagher team is utilising multiplex immunofluorescence and digital pathology to investigate the relationship between tumour-specific therapeutic and prognostic biomarkers and immune cell subsets in breast cancer tissue. Our fifth aim is to apply this methodology to NSCLC tissue to analyse the spatial relationship between lncRNA expression and immune cell markers.

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2. Esposito, R., Polidori, T., Meise, D. F., Pulido-Quetglas, C., Chouvardas, P., Forster, S., Schaerer, P., Kobel, A., Schlatter, J., ... Johnson, R. (2022). Multi-hallmark long noncoding RNA maps reveal non-small cell lung cancer vulnerabilities. Cell genomics, 2(9), 100171.
3. Chao, X., Wang, P., Ma, X., Li, Z., Xia, Y., Guo, Y., Ge, L., Tian, L., ... Guo, X. (2021). Comprehensive analysis of lncRNAs as biomarkers for diagnosis, prognosis, and treatment response in clear cell renal cell carcinoma. Molecular therapy oncolytics, 22, 209–218.
4. Yarmishyn, A. A., & Kurochkin, I. V. (2015). Long noncoding RNAs: a potential novel class of cancer biomarkers. Frontiers in genetics, 6, 145.
5. Lynch, S. M., Russell, N. M., Barron, S., Wang, C. A., Loughman, T., Dynoodt, P., Fender, B., Lopez-Ruiz, C., ... Gallagher, W. M. (2021). Prognostic value of the 6-gene OncoMasTR test in hormone receptor-positive HER2-negative early-stage breast cancer: Comparative analysis with standard clinicopathological factors. European journal of cancer (Oxford, England : 1990), 152, 78–89.

9

Family-Centred Cancer Care End of Life Education (FCCC-EoLEd)

Dr Carla O'Neill* [1], Sarah Sheehan [1], Dr. Jeffrey R. Hanna [2], Dr. Amanda Drury [3], Prof. Tanya McCance [2], & Prof. Cherith J. Semple [2].

1. *University College Dublin*
2. *Ulster University*
3. *Dublin City University*

Background: Adults with advanced cancer that have dependent children (>18) want guidance to communicate with their children when death is imminent. Health and social care professionals (HSCPs) are ideally placed to provide this aspect of care but lack the skills to do so due to insufficient training. This has a detrimental impact on the delivery of family-centred care and an adverse psychological impact for the family unit.

Objectives: The aim of the project is to systematically and iteratively develop, test and evaluate a novel, theory-driven and evidence-based eLearning resource to equip HSCPs to communicate with, and support families, when an adult with a significant caregiving responsibility for children is at end of life (EoL) from cancer.

Design: The project is employing a mixed method sequential study design using the 'person-based approach'.

Methods: The study, thus far, has undertaken a systematic review following Joanna Briggs Institute methodology and developed an e-Learning resource which is currently undertaking testing and refinement in line with the person-based approach intervention development framework.

Results: Two eligible studies were identified in the systematic review, highlighting the dearth of educational interventions available. Thus far, nine participants have piloted the developed eLearning resource and have provided feedback which has enabled modifications to enhance the resource.

Conclusion: There is a dearth of interventions available to equip HSCPs to support families when a parent is at EoL with cancer. We aim to provide an eLearning resource to provide a novel, theory-driven and evidence-based educational intervention to fulfil this need.

please visit our poster presenters to find out more about their projects.