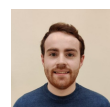


SSPC Cancer Spotlight 1

The design and delivery of new medicines for treating cancer, as well as understanding factors implicated in disease progression and relapse, represents an urgent clinical need. In Cancer Spotlight 1, we highlight frontier research undertaken by SSPC researchers in this field that is enabled and strengthened by deep collaborative ties, shared expertise, and access to world-class infrastructure established across the Centre. Significant progress in the click chemistry targeting and tracking of clinically approved, and pre-clinical platinum drugs is reported by research teams led by the Griffith lab in RCSI, and the Kellett group in DCU. In parallel, the O'Sullivan lab in DCU describes microRNA biogenesis in pancreatic cancer models to better understand disease progression and response to clinically approved combination chemotherapy treatments. Finally, we discuss "eRaDicate", a new Marie Skłodowska Curie Doctoral Network involving the Tajber laboratory at Trinity College Dublin. This interdisciplinary programme will develop and examine novel anti-cancer agents targeting nuclear receptors, with the long-term goal of eliminating cancer relapse. **Editorial: Professor Andrew Kellett**

The Development of a Bioorthogonal Toolkit for the Functionalisation of Clinical Platinum-based Anticancer Drugs



Dr Darren Griffith
Dr Paul O'Dowd
Royal College of
Surgeons Ireland

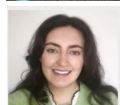
Cisplatin, Carboplatin and Oxaliplatin, approved worldwide and central to almost 50% of all cancer treatments, are examples of platinum anticancer complexes whose mechanisms are poorly understood. The focus of the research is to use innovative click and bioorthogonal chemistry to resolve the mechanisms of action and functionalise clinically relevant platinum drugs. One key output of this research was the production of a library of click functionalisable platinum anticancer complexes that can be conjugated further with fluorophores, peptides or other bioactive molecules.

Using click/bioorthogonal chemistry provided the means to functionalise platinum complexes with targeting/ tracking agents which can be used to circumvent resistance mechanisms and reduce off-target toxicity. Therefore the library can be used to better understand the mechanisms of action of clinically relevant anticancer drugs and limit drawbacks associated with their administration by reducing resistance and toxicity



Novel Platinum(II) Tetrazine Complex Capable of Live-Cell IEDDA Reaction. Paul D. O'Dowd, Dan Wu, Alby Benny, Ellen King, Alice Harford, Brendan Twamley, Olga Piskareva, Donal F. O'Shea, Darren M. Griffith, (2025), Vol. 26, *ChemBioChem*

Advanced Modelling of Pancreatic Cancer



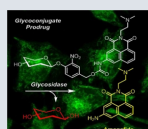
Associate Professor
Finbarr O'Sullivan
Dr Taylor Jade Coyle
Dublin City University

Better understanding of miRNA biogenesis and its contribution to disease state has societal and health benefits as there are currently no robust and reliable early detection methods for pancreatic cancer and the 5-year survival rate has not improved in over 40 years. This research project aimed to better understand combination chemotherapies administered to pancreatic cancer patients. By developing pharmacodynamic modelling in 2D & 3D pancreatic cancer cell cultures, the researchers were able to study the interactions among the triple combination FOLFIRINOX.

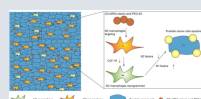
A stably miRNA overexpressing cell line panel was developed to better understand miRNA biogenesis in cancer cells which could lead to explanations for their dysfunctional expression in disease states. In addition, the project investigated the role of five novel miRNAs in disease progression, enabled by phenotypic analysis in conjunction with multiomic profiling using Quant-Seq and Mass Spectrometry.

miRNA- and Cell Line-Specific Constraints on Precursor miRNA Processing of Stably Transfected Pancreatic Cancer and Other Mammalian Cells. Taylor J Allen-Coyle, Berta Capella Roca, Alan Costello, Niall Barron, Joanne Keenan, Martin Clynes, Fiona O'Neill, Finbarr O'Sullivan, (2024), 25(11), 5666, *Int. J. Mol. Sci*

Publication highlights



Real-Time Multi-Photon Tracking and Bioimaging of Glycosylated Theranostic Prodrugs upon Specific Enzyme Triggered Release. Calatrava-Pérez, E., Marchetti, L.A., McManus, G.J., Lynch, D.M., Elmes, R.B.P., Williams, D.C., Gunnlaugsson, T., Scanlan, E.M., (2022), Vol. 28, *Chemistry - A European Journal*



Sialic acid-targeted cyclodextrin-based nanoparticles deliver CSF-1R siRNA and reprogram tumour-associated macrophages for immunotherapy of prostate cancer. Sun, Y., Cronin, M.F., Mendonça, M.C.P., Guo, J., O'Driscoll, C.M., (2023), Vol. 185, *European Journal of Pharmaceutical Science*

"eRaDicate" EU- project to Research Innovative Ligands for Nuclear Receptors to Eradicate Cancer Relapse

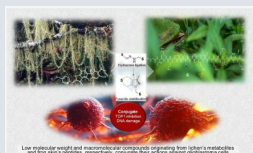


Professor Lidia Tajber
Trinity College Dublin

Professor Lidia Tajber from Trinity College Dublin, principal investigator in "eRaDicate" a Marie Skłodowska Curie Doctoral-Network (DN) which is an international, multi- & interdisciplinary and inter-sectoral training, research and development programme in the field of cancer drug research.

The scientific objectives of the project are to test novel anti-cancer agents, which target nuclear receptors, such as the retinoic acid receptor (RAR) and the vitamin D receptor (VDR), to develop innovative variants of these molecules, and to investigate the efficacy of different compounds against chemotherapy-induced neutropenia. In addition, strategies for the pre-formulation of active substances will be worked out and a novel deep-learning-based method for cancer analysis and diagnosis will be developed. The long-term goal is to translate the developed active substances into marketable drugs.

Publication highlights



Novel Peptide-Drug Conjugates with Dual Anticancer Activity. O'Flaherty, S., Luzina, O.A., Dyrkheeva, N.S., Krier, Y., Leprince, J., Zakharenko, A.L., Pokrovsky, M.A., Pokrovsky, A.G., Lavrik, O.I., Salakhutdinov, N.F., Varbanov, M., Devocelle, M., Volcho, K.P., (2024), Vol 25, *International Journal of Molecular Science*

The Design, Development and Analysis of Therapeutic Polynuclear Platinum(II) Complexes



Professor Andrew Kellett
Conor Newsome, PhD,
Dublin City University

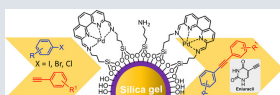
New platinum-based chemotherapeutic agents are essential for treating resistant cancers and improving survival and recovery in patients with aggressive tumors. This research project looks at design and synthesis of new targeted, low-dose anti-cancer polynuclear platinum(II) complexes (PPCs). The research involves enhancing the selectivity, trackability in biological environments such as cells, and stability of PPCs when bound to DNA. It couples PPCs with targeting therapeutic nucleic acids for enhanced specificity to diseased DNA and tissues using click chemistry to improve cellular uptake. Analysis is conducted on the interactions between PPCs with DNA and diseased cells, including conformational changes, binding and mechanism of apoptosis within various types of cancer cell lines.

The research looks at the synthesis of new DNA interacting dyes that have the ability to be coupled with PPCs, potentially stability of triplexes formed using triplex-forming nucleotides and provide trackability when administered to DNA and cells. Overall, the work seeks to advance platinum-based chemotherapies to improve cancer treatment outcomes.

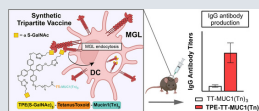
Nucleic Acids Research

A trackable trinuclear platinum complex for breast cancer treatment. Carroll, S., Slator, C., de Paiva, R.E.F., Newsome, C., Searle, B., Kk, S., Whittle, S., Catley, T.E., Scoditti, S., Mnich, K., Peterson, E.J., Hu, B., Koblinski, J.E., Samali, A., McKee, V., Pyne, A.L.B., Westerlund, F., Farrell, N.P., Kellett, A., (2025), Vol. 53, *Nucleic Acids Research*.

Publication highlights



A silica gel-supported schiff base palladium nanocatalyst for sonogashira cross-coupling and synthesis of an anti-cancer chemotherapeutic agent. Sarkar, S.M., Rahman, M.L., Hasan, K., Khan, M.M.R., O'Reilly, E.J., (2024), Vol.42, *Sustainable Chemistry and Pharmacy*



MUC1 Glycopeptide Vaccine Modified with a GalNAc Glycocluster Targets the Macrophage Galactose C-type Lectin on Dendritic Cells to Elicit an Improved Humoral Response. Adele Gabba, Riem Attariya, Sandra Behren, Christian Pett, Joost C. van der Horst, Hajime Yurugi, Jin Yu, Moritz Urschbach, Juan Sabin, Gabriel Birrane, Edgar Schmitt, Sandra J. van Vliet, Pol Besenius, Ulrika Westerlind, Paul V. Murphy, (2023), Vol. 145, *Journal of the American Chemical Society*

Meet the

SSPC
Experts

Professor Andrew Kellett
Professor Susan Quinn
Professor Abina Crean
Professor Caitriona O' Driscoll
Professor Damien Thompson
Professor Marc Devocelle
Professor Donal O' Shea
Professor Lidia Tajber
Professor Martin Clynes
Associate Professor Emmet O' Reilly
Professor Thorri Gunnlaugsson
Associate Professor Eoin Scanlan
Professor Paul Murphy
Associate Professor Constantina Papatriantafyllopoulou
Associate Professor Robert Elmes
Associate Professor Joanna McGouran
Associate Professor Matthias Vandichel
Professor Brendan Griffin
Associate Professor Paula Meleady
Associate Professor Finbarr O' Sullivan
Associate Professor Darren Griffith
Dr Katie Ryan
Dr Marco Monopoli
Dr Davide Tiana