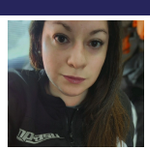
SSPC

Cancer Spotlight 2

Taighde Éireann Research Ireland

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 2, we highlight frontier research undertaken by SSPC researchers in this field. Our progress and research outputs are enabled and strengthened by deep collaborative ties, shared expertise, and access to world-class infrastructure established across the SSPC Centre. Leading this issue, the Kellett group at DCU, in collaboration with the Thompson group at UL, report significant advances in copper-mediated artificial metallo-nuclease design through CuAAC click chemistry, recently published in Nature Communications. The McGouran, Scanlan, and Gunnlaugsson laboratories at Trinity College Dublin describe complementary advances in targeted drug delivery, developing enzyme-responsive polymer platforms and tumour-selective naphthalimide-based agents. Next, the Griffin group at UCC reports progress in the formulation of oral oncology drugs through lipophilic salt strategies. Finally, the Crean group at UCC present an innovative microneedle-based platform for the topical delivery of vismodegib in the treatment of basal cell carcinoma, alongside work from the Papatriantafyllopoulou lab at the University of Galway on the synthesis of biocompatible metal-organic frameworks as versatile drug carriers.
Editorial: Professor Andrew Kellett

Expanding the DNA Damaging Potential of Artificial Metallo-Nucleases with Click Chemistry


Dr Alex Gibney, Dr Lily Arrué, Dr Shayon Bhattacharya, Professor Damien Thompson Professor Andrew Kellett

Recently, copper(I)-catalysed azide-alkyne cycloaddition (CuAAC) click chemistry has emerged as a promising approach for designing new artificial metallo-nucleases (AMNs) with DNA-damaging properties. By functionalising a central organic azide with three alkyne donors, Tri-Click (TC) ligands capable of chelating three copper ions through the donor group and triazole linker can be generated. However, the versatility of this approach along with the influence of specific donors on metal binding, DNA recognition, and cellular DNA damage in an anticancer context remains poorly understood.

Here, we prepare a series of Tri-Click ligands incorporating systematic cyclic and acyclic N-, O-, and S-donors and evaluate their AMN activities. Screening experiments pinpoint planar N-donor ligands as high value agents. Among these, the copper complex of Tri-Click-Pyridine (Cu_3-TC-Py) displays significant potential. Its activity was charaterised using single-molecule imaging, microscale thermophoresis, FRET-based binding assays, molecular dynamic modelling, and intracellular DNA interaction studies in human and functional bacterial cells. This paper reports the emergence of Cu_3-TC-Py as a high-value AMN with promising application for DNA damage applications central to anticancer therapy.

nature communications

Expanding the DNA damaging potential of artificial metallo-nucleases with click chemistry. Alex Gibney, Margareth Sidarta, Eva Delahunt, Pierre Mesdom, Lily Arrué, Sriram KK, Obed Akwasi Aning, Hedvig Hjerpe, Francisca Figueiredo, Kevin Cariou, Vickie McKee, Pegah Johansson, Shayon Bhattacharya, Damien Thompson, Michaela Wenzel, Gilles Gasser, Fredrik Westerlund & Andrew Kellett. (2026) *Nature Communications*

Tumour Responsive Systems for Targeted Drug Delivery


Associate Professor Joanna McGouran
Dr Connor O'Leary
Trinity College Dublin

The scientific community is continuously trying to improve the targeting of therapeutics with the aim of improving patient prognosis in cancer treatment. This body of research looked at producing a proof-of-concept study for a targeted enzyme-activated polymer-based drug delivery platform and to expand enzyme-activated/responsive systems to applications in medicinal chemistry and materials science. Its aim was to investigate the synthesis of compounds of carbohydrates conjugated to various polymerisable groups, polymerise these compounds (as a monomer or crosslinker) via two-photon polymerisation and conduct initial studies with β-glucuronidase to carbohydrate processing enzymes to observe a change in the physical properties of the polymer.

Naphthalimide Derivatives for Imaging and Targeting



Professor Thorri Gunnlaugsson, Associate Professor Eoin Scanlan
Dr Laura Ramierez
Trinity College Dublin

Many cancer drugs kills both cancer and healthy cells. This research project looked at developing tumour selective drugs by functionalising known anti-cancer drug molecules with targeting ones. The work involved developing a drug compromised of a RGD cyclic peptide moity as the targeting agent, a naphthalimide core such as the amonafide as the drug and a sugar to reduce toxic side effects.

This approach removes the drawbacks of the lack of selectivity from cancer treatments.

Design of Drug-Microneedle Formulations for the Treatment of Skin Cancer



Professor Abina Crean
Dr Sonja Vucen
Mohamed Elkhashab, PhD
University College Cork

Prof. Crean, Dr Sonja Vucen, and PhD student, Mohamed Elkhashab are investigating the development of an efficient topical treatment for basal cell carcinoma using a novel microneedle delivery system. This innovative approach leverages a patented micro-moulding technique to produce excipient-free microneedles to deliver a targeted cancer drug used for advanced basal cell carcinoma.

Their research aims to determine the structural, solid-state and chemical properties of the vismodegib microneedles (MN), investigate the structural, solid-state and chemical stability of the MNs under a range of storage conditions. It will establish whether administered in MN format can diffuse in the epidermis and dermis layer of the skin stopping basal cancer cells from growing and compare the pharmacokinetic profile of vismodegib MNs to a reference marketed product in a preclinical mode. This product would provide a minimally invasive alternative for treating basal cell carcinoma, improving patient outcomes and reducing the economic burden of healthcare associated with this prevalent form of skin cancer.

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

Designing Oral Oncology Medicines Free from the Food Effect


Professor Brendan Griffin
Callum Ryan, PhD
University College Cork

This research project looked at developing a food independent formulation for a recently licensed oral oncology drug and assess performance in- vivo in a porcine food effect model. It synthesised lipophilic salts of a BCS IV drug which displays a pharmaceutical food effect, so that it can be incorporated into a lipid-based formulation. The salts were characterised and their performance in a lipid vehicle assessed using several in-vitro tests. The project coupled computational tools with bio-predictive in-vivo screens to guide toward computationally informed formulation selection. The stability of lipophilic salts and impact on solubility were then assessed. Allowing typically inherently poorly soluble drugs to be incorporated into lipid-based formulations through conversion of the drug into a lipophilic salt, allows for a bioenabling technique (lipid-based formulation) to be used that would not have previously been possible. Development of a food independent formulation for oral oncology drugs results in improved patient compliance due to less restrictive dosage conditions.

Synthesis of Metal-Organic Frameworks for Drug Delivery


Associate Prof. Constantina Papatriantafyllopoulou
Dr Ahmed Ahmed
University of Galway

This project looked at the synthesis of highly porous biocompatible metal organic frameworks (MOFs) (zinc, copper, cobalt and magnesium nodes). It studied loading and delivery capability of anti-cancer drugs in novel MOFs and looks at developing antibacterial MOFs. The work included synthesis of MOFs based on elongated biocompatible linkers, studying loading of drugs such as rifampicin and doxorubicin and synthesis of MOFs containing antibiotic prodrugs as a component.

The research led to a better understanding of MOFs as drug carriers, including delivery capability (encapsulate and deliver drugs, proteins, enzymes, genes, or cells), and biocompatibility. They are excellent candidates in biomedical applications that involve drug delivery, enzyme immobilisation, gene targeting.

Publication highlights

scientific reports

Forecasting vaping health risks through neural network model prediction of flavour pyrolysis reactions. Akihiro Kishimoto, Dan Wu & Donal F. O'Shea, (2024), Vol. 14, *Scientific Reports*

Understanding the impact of silica nanoparticles in cancer cells through physicochemical and biomolecular characterizations. Saorin, A., Martinez-Serra, A., Paparoni-Bruzual, G.J., Crozzolin, M., Lombardi, V., Back, M., Riello, P., Monopoli, M.P., Rizzolio, F., (2024), Vol. 5, *Materials Advances*