Advances in Targeted Delivery for Hard-to-Treat Cancers

4th May 2023

Maxwell Centre, Cambridge

PROGRAMME

12:30	**Poster session and networking lunch**
13:30	**Welcome and introduction** *Prof George Malliaras, IRC Director*
13:40	**Local therapeutic delivery for brain cancer: an interdisciplinary approach** *Prof Ryan Mathew, University of Leeds*
14:00	**Bionic chemotherapy: Precision treatment of inoperable brain tumours** *Prof Rylie Green, Imperial College*
14:20	**Organic nanocarriers for drug delivery to solid tumours** *Prof Ljiljana Fruk, University of Cambridge*
14:40	**Q&A session**
15:00	**Coffee break and poster session**
15:30	**A chick egg model for testing therapies in mesothelioma** *Prof Judy Coulson, University of Liverpool*
15:50	**Supporting technology translation with manufacturing research** *Prof Ronan Daly, University of Cambridge*
16:10	**Q&A session**
16:30	**Wrap up and close** *Prof George Malliaras, IRC Director*
16:30-17:30	**Poster session and networking**

TALKS

Local therapeutic delivery for brain cancer: an interdisciplinary approach

Prof Ryan Mathew, University of Leeds

Glioma is a brain cancer of unmet need. Despite current best treatment, median overall survival remains dismal at 12-15 months. Maximal safe resection is the preferred first step in glioma management. However, the post-resection tumour cavity is surrounded by infiltrative cancer cells that resist adjuvant chemoradiotherapy and drive recurrence. Surgical targeting of these cells is limited by their intermingling with healthy and/or eloquent brain. Limited biological models exist to study this so-called 'margin zone.'

The Stem Cells and Brain Tumour Group at Leeds (co-led by Ryan Mathew and Heiko Wurdak), in conjunction with Academic Surgery, is working with partners in the IRC to utilise new, patient-derived in vitro and in vivo models to study the 'margin zone' and devise new local therapeutic interventions that can be deployed at the time of surgery. Examples include hydrogels, nanofibres and physically engineered devices.

Bionic chemotherapy: precision treatment of inoperable brain tumours

Prof Rylie Green, Imperial College

Bypassing the blood brain (BBB) to achieve localized drug delivery at the tumour site can be achieved by a physical device that penetrates the BBB. However prior attempts using fluid based technologies (convection enhanced delivery) led to increased intracranial pressure. Dry drug offloading removes the pressure but both wafer and gel technologies require a resection cavity in which the device can be placed, limiting the application to patients with accessible tumours.

Bionic chemotherapy circumvents these issues by enabling dry drug delivery (no liquid carrier) through a small gauge implantable device that can penetrate the tumour site. Electrical gradients are then used to drive the chemotherapeutic agent into the tissues in a controlled manner. This work focuses on the development of a conductive elastomer (CE) platform that enables the direct transfer of therapeutic molecules from the solid-state device. Studies have shown that both doxorubicin and cisplatin can be delivered in this manner and retain their chemotherapeutic potential against GBM cells. Using this unique delivery mechanism, bionic chemotherapy is positioned as an emerging treatment for brain tumours without the off-target effects seen with other local drug delivery techniques.

Organic nanocarriers for drug delivery to solid tumours

Prof Ljiljana Fruk, University of Cambridge

Modern molecular science is merging our knowledge of biochemistry, molecular biology, physics and even artificial intelligence to come up with materials that have a potential to take us into the era of precision medicine. Particular advances have been made in the design of bio-nano hybrids, which combine the biomolecules and man-made nanostructures and overcome intrinsic differences between individual elements.

A short talk will present the design of organic nanocarriers based on proteins and biocompatible polymers for delivery of drugs to solid tumours, in particular, pancreatic cancer. We will also look at the challenges within the field of nanocarrier design and what the future looks like for application of nanostructured materials in medicine.

A chick egg model for testing therapies in mesothelioma

Prof Judy Coulson, University of Liverpool

We have developed methodology for growing low-passage patient-derived malignant pleural mesothelioma (MPM) cell lines on the chorioallantoic membrane (CAM) of fertilised hen's eggs as 3D vascularised tumours. The MPM-CAM model recapitulates many aspects of human disease and is a cost effective, higher throughput alternative to murine xenograft models to translate in vitro studies of emerging therapeutic interventions. Drugs can be administered topically onto tumour nodules, or systemically via intravenous or yolk sac injection, with effects monitored by bioluminescence imaging and histology. We are evaluating the model's potential for testing novel delivery systems developed by IRC groups including hydrogels (Prof Scherman) and metal-organic frameworks (MOFs; Prof Fairen-Jimenez). We are investigating 1) optimal routes of administration, 2) any toxicity of the unloaded delivery systems on chick embryo survival, 3) uptake of delivery systems into MPM-CAM xenografts, and 4) efficacy of drug-loaded (e.g. platinum/pemetrexed) versus unloaded delivery systems in killing MPM-CAM xenografts. This biologically relevant preclinical model can provide a platform for pre-screening novel drug/delivery systems.

Supporting Technology Translation with Manufacturing Research

Prof Ronan Daly, University of Cambridge

The Manufacturing Cross-Cutting Theme within the EPSRC IRC in Hard-to-Treat Cancers identifies and explores underpinning scientific challenges that, when addressed, support translation of the targeted treatment technologies to the clinic. Here, we firstly present how to integrate technology-specific downstream challenges into research and secondly give examples of multidisciplinary research carried out within the theme to support both the IRC nanoparticle and implantable drug delivery technologies. The presentation concludes with a summary of key trends in medical device manufacturing and how they may influence future research.

SPEAKERS

Prof George Malliaras, IRC Director

George Malliaras is the Prince Philip Professor of Technology at the University of Cambridge. He received a PhD from the University of Groningen and did a postdoc at the IBM Almaden Research Center. Before joining Cambridge, he was a faculty member at Ecole des Mines de St. Etienne and at Cornell University, and served as the Director of the Cornell NanoScale Facility. His research has been recognized with awards from the New York Academy of Sciences, the US National Science Foundation, and DuPont. He is a Fellow of the Materials Research Society and of the Royal Society of Chemistry.

Prof. Malliaras leads a group of scientists, engineers and clinicians who study the fundamental processes at the abiotic/biotic interface and develop better tools for healthcare. He is interested in the development and translation of implantable and wearable devices that interface with electrically active tissues, with applications in neurological disorders and brain cancer.

Prof Ryan Mathew

Ryan Mathew is an Associate Professor at the University of Leeds and an Honorary Consultant Neurosurgeon at Leeds Teaching Hospitals. He obtained an MBCHB with Honours and an intercalated BSc with Honours, the latter in Clinical Sciences (Tissue Engineering) research. During his neurosurgical training at Leeds (FRCS (SN) in 2013), he undertook further basic science research (funded by CRUK) and was awarded a PhD based on Glioma Modelling using induced Pluripotent Stem Cells (iPSCs) and Cerebral Organoids. He has spent time as a Visiting Research Collaborator at the Brain Tumour Research Centre at Sickkids in Toronto.

His clinical practice covers the full spectrum of general neurosurgery with a subspecialty interest in brain tumours; in particular gliomas, meningiomas and awake surgery. His basic science research interests focus on developing advanced in vitro and in vivo brain tumour models, studying residual glioma cell populations that are resistant to therapy and fuel recurrence, and developing local therapeutic treatments. He also leads a research portfolio in surgical technologies and devices which encompasses virtual/mixed reality, machine learning for early brain tumour diagnosis and malignant transformation, real-time intra-operative tumour visualisation and histology, in silico trials, and early phase neoadjuvant and repurposing trials. He is the Neurosurgery Lead for the NIHR Surgical MIC, Surgical Technologies Academy Incubator and RCS Leeds Institute of Clinical Trials Research. He is a member of the Academic Committee of the SBNS, BNOS Research Subcommittee and a HoloMedicine Association Founding Member.

Prof Rylie Green

Rylie Green is the Head of Bioengineering at Imperial College London.
In her research, Prof Green has developed a range of innovative materials to address the limitations that hinder the development of next-generation bioelectronic devices. Her focus has been in developing electrode technologies that are stretchable and mediate improved electrical charge transfer with the body, including pioneering living bioelectronics. Prof Green has also developed wearable diagnostic devices and drug delivery systems for localised chemotherapy based on her conductive material technologies. This research has initiated collaborations with Galvani Bioelectronics, Cochlear Ltd and the US Department of Defense. Prof Green is an Associate Editor for APL Bioengineering, Advanced Bionanomedicine and Biomaterials.

Prof Ljiljana Fruk

Ljiljana Fruk is an Associate Professor of Bio-nano Engineering and her research is focused on design of biocompatible hybrid materials for use in catalysis/sustainable manufacturing and nanomedicine, particularly for drug delivery and biosensing. The focus of her research in nanomedicine are bioinspired drug delivery systems for hard-to-treat cancers such as pancreatic cancer and theranostic strategies to screen for and remove aged (senescent) cells. Her group pioneered use of photo-click chemistry for nanomaterial functionalization, and development of organic contrast agents for senescent cells.

Ljiljana studied chemistry at the University of Zagreb, obtained a PhD in bio-spectroscopy from University of Strathclyde, Glasgow (2000-2004), and worked on DNA structuring and enzyme reconstitution as a Humboldt and Marie Curie fellow at the University of Dortmund, Germany (2004-2008). Prior to joining the Department of Chemical Engineering and Biotechnology, she led a research group at Karlsruhe Institute of Technology (Germany, 2009-2014). She is an active science popularizer, art-science curator, and the co-author of the field-establishing Molecular Aesthetics book (MIT Press 2013), and the first textbook on Bio-nanotechnology (Cambridge University Press 2021).

Prof Judy Coulson

Professor Judy Coulson graduated from the University of Salford in Biological and Biochemical Sciences, and the University of London with a PhD in Biochemistry. She was a post-doctoral researcher at Aston and Nottingham Universities, before joining the University of Liverpool as a lecturer in 2001, and receiving the British Association for Cancer Research/AstraZeneca Young Scientist Award in 2003.

Judy is now the non-clinical Deputy Head of Department in Molecular and Clinical Cancer Medicine and the Academic Lead for the Liverpool Chick Egg Facility. She has served on scientific network and grant awarding committees, including currently for Mesothelioma UK. In 2022, Judy was appointed as Deputy Associate Pro Vice Chancellor for Technology, Infrastructure and Environment in the Faculty of Health and Life Sciences, and the Faculty Lead for Equality Diversity Inclusion and Wellbeing.

She leads an active cancer biology research group interested in deciphering the interplay between cell signaling, transcription and ubiquitylation, to identify potential new therapeutic approaches. A focus on mesothelioma led to the development of new preclinical chick egg models to test therapies for this hard to treat cancer.

Prof Ronan Daly

Ronan Daly is Professor of Advanced Manufacturing in the Department of Engineering, University of Cambridge. He is a Course Director for the Manufacturing Engineering course, where students learn about manufacturing technologies and manufacturing management.

He previously worked in Unilever R&D before completing a PhD in Chemistry from School of Chemistry and Centre for Research on Adaptive Nanostructures and Nanodevices, Trinity College Dublin.

He leads the *Fluids in Advanced Manufacturing* research group, which tackles the fluid flow and functional material challenges to enable scale-up of advanced technologies to manufacturing.