BRS

BIOLOGICAL RESEARCH SOCIETY

16TH ANNUAL RESEARCH DAY 2025

ABSTRACT BOOK

Welcome to the Biological Research Society's 16th Annual Research Day 2025!

We are delighted to have so many of you participate and hope you enjoy the research talks we have scheduled throughout the day. This year we are very excited to be able to invite back sponsors and to be able to create a day for all researchers in the School of Biotechnology and Life Science Research Institute (LSRF) with great opportunities to network.

The BRS Committee would like to thank: our generous sponsors for supporting the work of the BRS committee and Research Day, Dr. Alex Eustace and Mary Rafter for their continuous support throughout the whole organization process; the professors at School of Biotechnology and LSRF who so kindly volunteered to chair/judge the sessions planned and most importantly, the researchers without whom this day would not be possible.

We hope you enjoy the fascinating research talks scheduled and we encourage you all to engage with our sponsors and have fun!

BRS Committee

(2024 – 2025)

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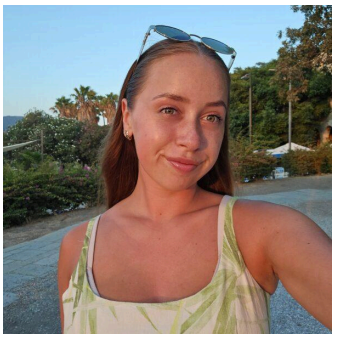

Karina Kulakova

Panagiotis Sarametidis

Daphni Doulaptsi-Teeuwen

Eolas Award

This year marks the launch of the Eolas Award, introduced by the BRS Committee to support outstanding early-career researchers. The first recipient, Margherita Obinu, a second-year PhD student, will attend the first EACR Cancer Neuroscience Conference, taking place in Bilbao, Spain, 14-16 October 2025.

Prostate Cancer-Nerve Interactions: Unlocking Novel Biotherapeutic Strategies

Margherita Obinu

Introduction: Prostate cancer (PCa) is the most common malignancy in men. The prostate's growth and function are regulated by hypogastric and pelvic nerves, which also influence PCa progression. Nerve-cancer interactions, including perineural invasion, enhance cancer survival, aggressiveness, pain, and sensory dysfunction. Understanding these interactions may help identify therapeutic targets, such as botulinum neurotoxin (BoNT), to reduce PCa-related pain.

Methods: Bioinformatics analysis of patient and cell line data using cBioPortal and DepMap identified genes linked to neuronal signalling, some with higher expression in advanced PCa. To assess neurotrophic signalling, conditioned media (CM) from three PCa cell lines was applied to PC12 cells, and neurite outgrowth was evaluated.

Results: Bioinformatics analysis identified key factors, including NGF, TGFβ1, BoNT receptors, such as STX1A, SNARE proteins, which were differentially expressed in aggressive PCa. PC12 cells exposed to CM showed neurite outgrowth, with DU145 inducing the strongest effect. This aligns with bioinformatics findings, as DU145 originates from a brain metastatic lesion, representing aggressive PCa.

Conclusions: This study explores neurotransmitter and BoNT receptors in PCa cell lines to identify therapeutic targets and examines neurotrophic signalling between PCa and PC12 cells, highlighting secreted neuro-neoplastic factors in PCa.

Topics: Prostate Cancer, Cancer-Nerves Interactions, Pain, Neuro-oncology

Development of ErbB gene mutated breast cancer cell models using a CRISPR/Cas 9 gene editing approach

Anita White

Breast cancer (BC) is the most common cancer occurring in women worldwide and in Ireland there are, on average, 3,700 new cases of BC diagnosed each year.

Based on molecular characteristics BC can be categorised into four subtypes: Luminal A which corresponds to Hormone receptor (HR) positive (Estrogen Receptor (ER+), Progesterone Receptor (PR+), Human epidermal receptor 2 (HER2-); Luminal B , positive for one or both of the HRs and HER2 +/-.The third and fourth subtypes are known as HER2+, where overexpression of HER2 occurs and triple negative breast cancer (TNBC) (ER-,PR-,HER2-).

The HER2 protein belongs to a family of four transmembrane proteins with tyrosine kinase activity, and are encoded by the ErbB gene family. From two large clinical databases I have identified the most prevalent somatic missense mutations occurring in the ErbB gene family within breast cancer patient cohorts, based on likelihood for functional impact and I want to investigate further their importance as cancer driving mutations. The prevalence of these mutations highlights the implication of this family of genes in cancer that are outside the HER2 overexpression phenotype.

The study aims to introduce the selected mutations into BC cell lines using the CRISPR/Cas 9 gene editing approach with the view to using the modified cell lines to study the impact of a mutation on cell behaviour, expression of key signalling pathway proteins and to screen drugs targeting the HER protein family and PI3K pathway.

Topics: Breast cancer, Somatic mutations, CRISPR/Cas 9 genome editing, ErbB gene family

FLASH FIVE PRESENTATIONS

Applying Genomics to the challenge of ending Tuberculosis in Ireland

Cian Ennis

Tuberculosis (TB) is now the leading cause of death from a single infectious agent worldwide. In 2023, the World Health Organisation reported 10.8 million cases of TB, with an estimated 400,000 of which being Multi-drug resistant (MDR) or rifampicin-resistant (RR). Drug-resistant TB (DR-TB) is estimated to account for one in three deaths associated with antimicrobial resistance globally. Furthermore, mathematical modelling has forecasted that MDR-TB, as a proportion of total incident TB cases, is likely to rise in the coming years.

Our preliminary analysis focused on exploring a large dataset of Mycobacterium tuberculosis genome sequences to improve our understanding of the drivers of MDR-TB in Ireland and overseas. Using core-genome multi-locus sequence typing and whole-genome variant analyses, we identified two major lineages contributing most to Ireland's MDR-TB burden, each displaying distinct geographical patterns of association within the transmission-associated 12 SNP-distance threshold. This work highlights the utility of genomics in TB surveillance and contributes to a deeper understanding of DR-TB transmission dynamics in low-burden countries such as Ireland.

Topics: Tuberculosis, Genomics, Antimicrobial Resistance, Epidemiology

FLASH FIVE PRESENTATIONS

Using digital droplet PCR to validate RPA-CRISPR-Cas assay for potato blight detection from eDNA aerosol samples

Ciara McDermott

Potato late blight, caused by *Phytophthora infestans*, threatens global potato production, with annual losses of €1 billion across Europe and €5 million in fungicide costs in Ireland. Since the co-emergence of the A1 and A2 mating types of *P. infestans*, there has been a spike in fungicide resistant strains in Europe. Current detection methods rely heavily on PCR technology but can't keep up with the airborne spread of the pathogen, leaving potato growers without timely information as the disease progresses.

The Research Ireland Food Challenge project, AgSENSE (Agricultural Fungal Sensing) aims to develop a rapid, strain-specific detection system to identify *P. infestans* eDNA before visible symptoms appear. An RPA-CRISPR-Cas assay with a lateral flow colorimetric readout, allows potato growers to sample a potato leaf or an air filter and receive a diagnosis within 1 hour on-site.

The use of environmental DNA (eDNA) means the mitochondrial genome of *P. infestans* is targeted, due to its stable circular structure and high copy number. This minimises the risk of DNA degradation from environmental samples. To ensure assay robustness, validation and optimisation using a digital droplet PCR is critical for this novel plant pathogen detection system.

Through collaboration with key agricultural stakeholders including Teagasc, AgSENSE aims to integrate a more applicable detection method to revolutionise agricultural disease maintenance practices.

Topics: Plant Pathogen Detection, Digital droplet PCR assay design, Potato Late Blight, Sustainability practices

Feeding assays unravel the impact of pollutants on daphnids

Emma Rowan

Traditional approaches for monitoring aquatic pollution primarily rely on the detection of pollutants in aqueous environments. However, these methods lack realism and mechanistic insight, thus, prompting a shift towards effect-based methods which provide sensitive endpoints for risk assessment. In this context, daphnids, a freshwater species extensively used in molecular ecotoxicology, offer rapid and non-invasive approaches to assess the impact of pollutants. Among the phenotypic endpoints used, feeding rate is particularly sensitive, as it can indicate physiological alterations even at sublethal concentrations.

Feeding rate, for which there has been no standardised method, and existing assays often require large volumes, extensive incubation times, and high animal densities or employ complex techniques such as fluorescence, radiolabelling, or direct counting of ingested cells. These methods can be challenging and labour-intensive, necessitating cumbersome instrumentation. To address these limitations, we developed high-throughput methods to assess feeding as the ingestion of fluorescent microparticles.

Two optimised approaches were optimised and tested on daphnids following exposure to non-lethal concentrations of a range of pollutants. Our findings demonstrated that this new approach could detect significant differences in daphnid physiology even at concentrations below toxicity limits for various pollutants with different modes of action.

Topics: Daphnia magna, Toxicity, Feeding rate, Fluorescence, Miniaturisation

FLASH FIVE PRESENTATIONS

Investigating new therapeutic modalities for atypical teratoid/rhabdoid tumor using *in vitro* models

Jessica Alyas

Atypical teratoid/rhabdoid tumors (AT/RT) are highly aggressive pediatric brain tumors with limited treatment options and poor prognosis. Effective therapies are urgently needed but the presence of the blood-brain barrier (BBB) and high recurrence rates make therapeutic targeting challenging. AT/RT comprises three molecular subtypes: SHH, MYC, and TYR. This project assesses new therapies for AT/RT using HER-family targeting antibody-drug conjugates, tyrosine kinase inhibitors, and the Aurora kinase A inhibitor alisertib in different AT/RT cell lines. Western blot revealed Aurora A and EGFR expression in all cell lines. HER2 was expressed in CHLA-04, CHLA-06, BT-12, and BT-37; HER3 was absent in all cell lines; HER4 was seen in CHLA-04, CHLA-05, CHLA-06, and BT-37. Alisertib showed dose-dependent efficacy in CHLA-04 and CHLA-06 (IC50: 1.23±0.8 µM, 2.94±1.2 µM), while neratinib was effective in CHLA-05 (IC50: 0.98±0.2 µM). Lapatinib showed no efficacy. These findings suggest that AT/RT-SHH and AT-RT-MYC cell lines are inhibited by the Aurora kinase A inhibitor alisertib, while neratinib displayed the greatest anti-proliferative effect in a model of the AT/RT-SHH subtype. Next, 3D brain-like tumor models incorporating BBB features will be developed to assess if these drugs can penetrate the BBB and their combinatorial efficacy, followed by AUTOPILOT-based compound screening and in vivo validation. The ultimate goal is to identify safe, targeted therapies for AT/RT.

Topics: Pediatric Brain Tumors, Targeted Cancer Therapies, Aurora Kinase A Inhibition, HER-Family, Tyrosine Kinase Inhibitors, AT/RT Subtype-Specific Drug Response

RESEARCH TALKS

The interplay between CD4+ T cells autophagy, metabolism and fitness in Rheumatoid arthritis

Daphni Doulaptsi-Teeuwen

Rheumatoid Arthritis (RA) is an autoimmune disease that affects the joints. T-cells are key mediators of disease pathogenesis and progression. Although synovial CD4+ T-cells have an exhausted phenotype, they surprisingly exhibit increased fitness in the hypoxic environment of the inflamed joint. Autophagy is a mechanism that maintains the cells during states of stress. We hypothesize that autophagy contributes to T-cell survival and RA progression.

To examine the role of autophagy in CD4+ T-cells in RA and its effect on their metabolism, fitness and function, single-cell RNA sequencing data of synovial tissue biopsies were analysed. Patients with RA T cells with an exhausted phenotype show increased utilisation of the autophagy pathway compared to HC derived exhausted T cells. Culture of T-cells in the presence or absence of autophagy inhibitors (BafA1, 3MA) or promoter (Torin1) followed by flow cytometric analysis for LC3B, WB and PCR analysis showed differential dependency on autophagy between RA patients and HC activated T-cells. Cell metabolism and production of pro-inflammatory cytokines were evaluated utilizing flow cytometric based techniques. The activity of the early and late autophagic pathway in T-cells from patients with RA is dysregulated.

The altered autophagic activity leads to functional and metabolic adaptations of the T cells in patients with RA. These observations give rise to new potential therapeutic targets that may help combat disease progression.

Topics: Rheumatoid Arthritis, CD4+ T-cells, Autophagy, Fitness

RESEARCH TALKS

Macrophage Plasticity drives Progression of Inflammation in Patients with Rheumatoid Arthritis

Karina Kulakova

Rheumatoid Arthritis (RA) is a progressive, chronic inflammatory disease of the joints with no cure. Synovial macrophages strongly correlate with disease activity, are highly plastic, and have a dual role in synovial inflammation.

The study aims to investigate the impact of macrophage plasticity on disease progression in RA. Surprisingly, single-cell RNA sequencing analysis of RA and HC synovial tissue shows similar proportions of macrophage subsets between patients with RA and HC. However, patients with RA M2a, M2b and M2d but not M2c macrophage subsets, while remaining transcriptomically distinct, share a high level of similarity with M1 macrophages. To assess how the hypoxic environment of the inflamed joint may drive M2 subsets towards M1-like macrophages, monocyte-derived macrophages from patients with RA and HC were polarised towards M1, M2a, M2b, M2c, and M2d under atmospheric O2 and hypoxic conditions. PCR, flow cytometry, flow-based ELISA and metabolic analysis revealed distinct, subset-specific changes in M2 macrophages and a switch towards an M1-like phenotype.

In vitro, polarised macrophages demonstrate evident plasticity in patients with RA compared to HC in response to environmental stimuli and shifts in metabolism in both M1 and M2 macrophages, allowing for highly proinflammatory phenotypes to emerge. Hence, an approach to maintain the stability of M2 macrophage subsets and re-establishing homeostasis may be an effective therapeutic option for RA.

Topics: Rheumatoid Arthritis, Macrophages, Plasticity, Disease Progression

RESEARCH TALKS

Pre-clinical Evaluation of T-DXd plus AZD1390 in Triple-Negative Breast Cancer Models

Larissa Bless

Triple negative breast cancer (TNBC) is the most aggressive breast cancer subtype. Antibody-drug conjugates (ADCs) offer a novel treatment approach. Trastuzumab deruxtecan (T-DXd), a HER2-directed ADC with a topoisomerase I-inhibiting payload, induces DNA double strand breaks (DSBs). Ataxia-telangiectasia mutated (ATM) kinase, a key player in DSB repair, can be inhibited to enhance DNA damage accumulation, providing a strong rationale for combining T-DXd with ATM inhibition in TNBC. We investigated T-DXd plus the ATM inhibitor AZD1390 in eight TNBC cell lines using 2D and 3D bio-printed models. Synergy of the combination was assessed through proliferation assays and further characterised by apoptosis induction via live-cell imaging, and DNA damage evaluation using fluorescence microscopy. Half-maximal inhibitory concentration (IC50) of T-DXd and AZD1390 single agents were achieved in all cell lines. The combination showed no antagonism but strong synergy across clinically relevant concentrations. Response in 3D models mirrored 2D cultures, with no difference in drug sensitivity.

Live-cell imaging confirmed that combination treatment significantly increased apoptotic cell death compared to single agents. T-DXd plus AZD1390 demonstrates strong synergy in reducing cancer cell growth, even at low nanomolar concentrations, supporting its potential to enhance targeted therapies for TNBC.

Topics: TNBC, Antibody-Drug conjugates, DNA Damage, Targeted therapy

RESEARCH TALKS

Exploring the role of Lipoxin (LXA4) as a novel therapeutic for chronic wound infections

Salini Mohapatra

Chronic wound infections are a major healthcare concern due to delayed healing, persistent inflammation, and rising antimicrobial resistance. Biofilm-forming pathogens like Staphylococcus aureus and Pseudomonas aeruginosa play a key role by increasing antibiotic tolerance and evading immune responses. There is a growing need for alternative therapies that target inflammation and promote healing. Lipoxins, specialized pro-resolving mediators derived from arachidonic acid, have shown promise in modulating immune responses and enhancing tissue repair. Synthetic lipoxin mimetics (sLXMs) have been developed to improve their therapeutic potential.

Initial in vitro experiments revealed that LXA4 treatment modestly reduced P. aeruginosa PAO1 biofilms, but had no significant impact on S. aureus biofilms. The observed effects in S. aureus were similar to ethanol vehicle controls, suggesting minimal direct anti-biofilm activity. To overcome this limitation and better assess therapeutic relevance, we will use NativeSkin®, a live human skin model, to simulate chronic wound conditions. This model will allow us to establish S. aureus-infected wounds and evaluate lipoxin effects on infection dynamics, host response, and healing.

This study aims to explore the potential of lipoxin-based therapies as novel, resolution-targeted strategies for managing chronic wound infections, with a focus on improving outcomes in the face of escalating antibiotic resistance.

Topics: Chronic Wound Infections, Biofilms and Antimicrobial resistance associated with It, Lipoxin as a novel therapeutic

EARLY CAREER RESEARCHER PRESENTATION

The impact of chemical and commercial NSAIDs on Daphnia magna

Anna Michalaki

Non-steroidal anti-inflammatory drugs, such as indomethacin and ibuprofen, are abundant pollutants in the freshwater ecosystems due to their widespread use, raising concerns about their ecological effect. Despite the existing literature about the effects of NSAIDs on aquatic organisms, the impact of their both chemical and commercial forms using transgenerational exposures still remains inadequate. This study focuses on the evaluation of the impact of chemical and commercial forms of indomethacin, ibuprofen and their 1:1 mixture on Daphnia magna. Daphnids were exposed for four generations at environmentally relevant concentration of 5 µg/L and toxicity curves, followed by a recovery generation. Toxicity curves, enzyme activities and metabolomic analysis were used to evaluate the effect of the exposures. Results showed alteration in the activities of βGAL and LIP, while the effects were reversed in the subsequent recovery generation. A targeted LC-MS/MS approach revealed the distinct metabolic fingerprint caused by the chemical and commercial NSAIDs on the fourth generation of daphnids. This study highlights the importance of transgenerational exposures as an approach to comprehend the effect of pharmaceuticals at low concentrations, using molecular responses of physiology.

Topics: Ecotoxicology, Daphnia magna, metabolomics, NSAIDs

EARLY CAREER RESEARCHER PRESENTATION

Evaluation of RALA peptide nanoparticles for delivery of nucleic acids into human T-cells

Conor Lawlor

My PhD project explored whether RALA peptide nanoparticles deliver nucleic acids encoding GFP or Chimeric Antigen Receptors (CAR) into human T-cells as an alternative to viral vectors. RALA successfully delivered plasmid DNA (pDNA) or mRNA encoding GFP into the Jurkat T-cell line with similar transfection efficiencies of 15-30%. RALA outperformed other non-viral delivery platforms but was not as efficient as electroporation. However, RALA was not successful in facilitating the expression of pDNA encoding CARs which are larger compared to pDNA encoding GFP. Intriguingly, RALA delivered pDNA encoding GFP into 100% of T-cells, yet only 15-30% of the cells expressed this reporter, which led us to explore whether endogenous biological barriers limit transgene delivery and expression. We found that pre-treatment of Jurkat T-cells with endosomal/lysosomal disruptors increased RALA-mediated GFP expression by two-fold. Endogenous nucleic acid sensors also limited GFP expression, as inhibition of these sensors increased RALA-mediated GFP expression by two-fold.

A combination of an endosomal/lysosomal disruptor with inhibition of nucleic acid sensors increased transfection efficiencies further (GFP expression) and resulted in detectable CAR expression. These studies demonstrate that RALA can deliver nucleic acids encoding GFP or CAR into Jurkat T-cells but that biological barriers within endosomal/lysosomal pathways and nucleic acid sensors limit transgene delivery and expression.

Topics: CAR T-cell therapy, T-cell transfection, Non-viral delivery agents, Cell-penetrating peptides

EARLY CAREER RESEARCHER PRESENTATION

Investigating the Transportation and Storage of Zinc in Epithelial Cells

Martha Faulkner

Our skin cells require zinc as a micronutrient for healthy wound healing, immune protection, antioxidant defence and anti-inflammatory response. While the cellular response to zinc deficiency is well studied, there is less data available on the response to high zinc levels.

This study aimed to investigate, the cellular response of the human, HaCaT keratinocyte cell line to zinc from inorganic and organic sources. The HaCaT cells were also adapted to generate a zinc tolerant variant 'HaZT' which grew at concentrations of 550µM organic zinc. The zinc tolerant HaZT cells were characterised to reveal mechanisms used by skin cells to maintain zinc homeostasis. Such mechanisms included changes in expression of zinc transport proteins, a rapid efflux of zinc, and an increased expression of zinc storage protein metallothionein-1 (MT1).

Topics: Zinc, Metal ion transport, Skin health, Metal Ions

EARLY CAREER RESEARCHER PRESENTATION

Using CRISPR/Cas9 to edit KRAS in a small cell lung cancer cell line

Myra Castel

Introduction: An effective combination of drugs has been identified in 2 cancer cell lines that harbour both a HER2 amplification and a KRAS G12C mutation. However, they are the only two commercially available models with this specific genetic profile. This study aimed to engineer a HER2-amplified small cell lung cancer (SCLC) cell line, NCI-H1048, using CRISPR/Cas9 to insert the KRAS mutation.

Methods: A single guide RNA (sgRNA) near the mutation site was designed using SnapGene. Its efficiency and specificity were determined using CRISPRon and CRISPRoff webservers. A repair template with the nucleotide substitution was created. The CRISPR/Cas9 plasmid pSpCas9(BB)-2A-GFP (PX458, Addgene) was used. NCI-H1048 cells were transfected with either the sgRNA-containing PX458 (pKRASm) or the empty PX458 (control) using Lipofectamine 3000. GFP-positive cells were sorted and seeded for colony formation. Isolated pKRASm and PX458 clones were Sanger sequenced to determine KRAS G12C status. CRISPR gene editing outcomes were analysed using Synthego Ice and SnapGene.

Results: The transfection efficiency was 0.6% for pKRASm and 1.2% for PX458. No clones with a KRAS G12C mutation were isolated. However, 11 clones had deletions (1 to 103 bp) in KRAS exon 2, affecting different regions of KRAS.

Conclusion: This CRISPR/Cas9 method resulted in the creation of novel SCLC cell lines with KRAS alterations, but further optimisation of the protocol is needed to introduce KRAS point mutations.

Topics: Gene editing, CRISPR/Cas9, method development, cancer models

EARLY CAREER RESEARCHER PRESENTATION

Dissecting antagonistic function of phytic acid on zinc absorption in vitro

Niamh Rock

Zinc is an important trace metal, requiring daily dietary intake. However, zinc ingested does not equate to zinc absorbed by the body. Antagonists in the diet such as phytic acid (IP6) reduce the absorption of divalent metals such as zinc in vivo through the formation of stable complexes. A standardised in vitro digestion was optimised to study the inhibitory effect of IP6 on zinc absorption. The bioaccessibility and bioavailability of inorganic and organic zinc sources were compared following digestion. This revealed inorganic zinc to be more susceptible to IP6 complex formation. To assess if the presence of IP6 has an impact on the bioavailability (what intestinal cells can absorb), two intestinal cell lines (Caco-2 and IPEC-J2) were exposed to equimolar concentrations of zinc digests. These studies showed that cellular zinc uptake and toxicity assays for both cell lines showed no difference after digestion with or without IP6. This suggested the biggest impact of IP6 on zinc absorption is at the level of bioaccessibility and that organic zincs are less susceptible to IP6 interactions. Brodkorb, A. et al. (2019). INFOGEST static in vitro simulation of gastrointestinal food digestion. Nature Protocols. doi:10.1038/s41596-018-0119-1.

Topics: Zinc, Phytic acid, In vitro digestion, Bioaccessibilty, Bioavailability

Influence of SARS-CoV-2 Spike Protein Subunits on Potential Receptors of Diabetic Lung Endothelium

Niamh Donnelly

In December 2019, severe pneumonia cases caused by a novel coronavirus emerged, leading to a global pandemic that resulted in 778 million confirmed cases and 7.1 million deaths worldwide. SARS-CoV-2, commonly known as Covid-19, infects human cells in two distinct phases. Early entry involves initial viral-host contact and membrane fusion, while late entry endocytosis internalises the viral genome. The viral vesicle then reaches the cytoplasm, releasing the viral genome to promote replication. The spike glycoprotein of SARS-CoV-2 contains two subunits, S1 and S2, that are functionally distinct.

S1 facilitates the initial recognition and binding to host cell receptors, leading to viral transmission and pathogenesis. S2 anchors the spike protein to the viral membrane and facilitates membrane fusion, allowing the viral RNA to be released into the host cell's cytoplasm and use the cell's machinery to replicate new viral particles via endocytosis.

Research indicates that Covid-19 patients with controlled blood glucose levels face a reduced risk of complications compared to those with poorly controlled blood glucose levels. In particular, controlling blood glucose in individuals with type 2 diabetes may help predict the severity and outcomes of Covid-19. This study aims to explore the impact of SARS-CoV-2's S1 and S2 subunits on the gene expression of both well-known and novel receptors of the virus in hyperglycaemic environments.

Topics: SARS-CoV-2, Covid-19, Spike Protein, Cell Biology, Diabetes

Investigating the Transportation and Storage of Zinc in Epithelial Cells

Martha Faulkner

Our skin cells require zinc as a micronutrient for healthy wound healing, immune protection, antioxidant defence and anti-inflammatory response. While the cellular response to zinc deficiency is well studied, there is less data available on the response to high zinc levels.

This study aimed to investigate, the cellular response of the human, HaCaT keratinocyte cell line to zinc from inorganic and organic sources. The HaCaT cells were also adapted to generate a zinc tolerant variant 'HaZT' which grew at concentrations of 550µM organic zinc. The zinc tolerant HaZT cells were characterised to reveal mechanisms used by skin cells to maintain zinc homeostasis. Such mechanisms included changes in expression of zinc transport proteins, a rapid efflux of zinc, and an increased expression of zinc storage protein metallothionein-1 (MT1).

Topics: Zinc, Metal ion transport, Skin health, Metal Ions

CRISPR-Cas-mediated monitoring of Phytophthora infestans using environmental DNA in bioaerosols

Weili Guo

Fungi and oomycetes are major crop pathogens that threaten global food security due to their ability to disperse through the atmosphere. As a historically devastating and re-emerging oomycete pathogen, Phytophthora infestans (late blight) has continuously caused severe losses in potato production. The AGSENSE (Agricultural Fungal Sensing) project, supported by Research Ireland the National Challenge Fund, aims to protect crop yields by providing a forecast system with molecular techniques to monitor Phytophthora infestans. Current qPCR-based detection methods are labour-intensive, require sophisticated equipment and delay decision-making. Extensive engagement with stakeholders and end-users has identified an urgent need for on-site tools capable of detecting resistant strains in bioaerosols and leaves.

Given the insights from stakeholder engagement, we developed an environmental DNA (eDNA)-based assay using CRISPR-Cas12a integrated with real-time fluorescent and end-point colorimetric lateral flow detection platforms to identify Phytophthora infestans in bioaerosols. The assay demonstrated high specificity by distinguishing Phytophthora infestans from three closely related species. It exhibited a sensitivity of 0.85 fM within 30 minutes of Cas12a cleavage activity and detected Phytophthora infestans in 1 out of 17 eDNA samples. The assay's compatibility with lateral flow platform supports its potential as a rapid and field-deployable tool for plant pathogen detection.

Topics: Environmental DNA, CRISPR-Cas, Phytophthora infestans, Late Blight, Bioaerosols

Single-Cell Transcriptional Profiling of Vascular Endothelial Cells from Patients with Atopic Dermatitis

Michael Kitching

Previous studies have shown that atopic dermatitis (AD) skin is characterised by dysfunctional endothelial cells (ECs). However, their role in AD is understudied. Our group has demonstrated that genes involved in vesicular trafficking are responsible for the release of potent itch-inducing proteins in lesional atopic dermatitis (LAD) skin. However, it is unclear whether vesicle trafficking, specifically in ECs, is impacted in LAD. We utilised scRNAseq datasets from healthy controls (HC), LAD, and non-lesional (NLAD) from human AD patients to investigate whether the expression of genes involved in (i) vesicular trafficking, (ii) antioxidant defence, and (iii) EC function is altered in AD patients.

scRNAseq datasets were downloaded from the NCBI website (accession code GSE147424). ECs were identified by the expression of Pecam1, Vwf, and Cldn5. Gene expression differences were assessed using the Kruskal-Wallis test, followed by Dunn's multiple comparison post hoc test.

Three EC populations, two venous (VPC) and one capillary (CPC), were identified. VPC and CPC increased approximately threefold in NLAD compared to HC, but not in LAD. In CPCs from LAD, vesicle trafficking genes were upregulated. Additionally, the genes involved in the antioxidant response and endothelial function are upregulated in CPCs derived from NLAD. These findings demonstrate there are distinct transcriptomic profiles in ECs in both lesional and non-lesional skin, warranting further investigation.

Topics: Immunology, allergy, single-cell transcriptomics, vascular biology

UNDERGRADUATE POSTERS

The impact of pharmaceuticals on daphnids - A molecular approach

Izabela Antepowicz and Patrick Nedelea

Pharmaceutical pollution has become a great threat to the environment and inhabiting aquatic biota. Nonsteroidal anti-inflammatory drugs (NASIDs) and beta blockers are major pharmaceutical pollutants with significant presence in aquatic ecosystems. In this study, two NSAIDs, acetylsalicylic acid, and diclofenac, and two beta blockers, propranolol, and diltiazem were assessed on daphnids. Toxicity and survival were assessed to guide the selection of nonlethal concentrations for further investigation. Markers of physiology such as key enzyme activities were used to determine the impact of pharmaceuticals at a molecular level. Enzyme activities of phosphatases, lipase, aminopeptidase, and b-galactosidase were significantly impacted upon chronic exposure to pharmaceuticals. Feeding was measured as ingestion of microparticles and was used as a physiological endpoint. Overall, this study provides mechanistic insight regarding the toxicity thresholds of pharmaceuticals and highlights the need towards sensitive markers for pollution assessment in chronic scenarios and at environmentally realistic concentrations.

Topics: Pharmaceutical pollution, markers of physiology, and molecular ecotoxicology

Using Neural Networks To Understand Gene Regulation In the MCF-7 Breast Cancer Cell Line

Faith Ogundimu

Chromatin accessibility is a key regulator of gene expression, dictating transcription factor (TF) binding and transcriptional activity. Predicting accessible regions from histone modifications and TF signals is crucial for understanding cancer-specific regulatory dynamics.

However, many studies rely solely on AUC-ROC, overlooking performance metrics like MCC and F1 Score, which are more informative in imbalanced cancer datasets.

Accessibility is highly cell type-specific, with predictive histone marks and TF signals varying by context. This study develops and benchmarks machine learning and deep learning models for predicting chromatin accessibility using public histone modification, TF binding, and ATAC-seq data from the MCF-7 breast cancer cell line (ENCODE).

A neural network was trained on histone and TF features, outperforming an existing model that also incorporates motif and sequence data (Zhao et al., 2022), despite using fewer inputs.

The model appears to be the first to predict accessibility using only histone and TF binding data, highlighting regulatory drivers of cancer gene expression. Feature importance analysis identified H3K4me1 as the top predictor, consistent with its role in enhancer priming.

Future work will integrate RNA-seq to link accessibility to expression, expand to other breast cancer lines, and explore potential drug targets and chromatin velocity to predict dynamic state transitions.

Topics: Machine Learning, Breast Cancer, Artificial Intelligence, Epigenetics, Genetics, Drug Discovery

Human Brain Microvascular Endothelial Cell: In Vitro Inflammation Model

Gabriel Pascale

Background: Blood-brain barrier (BBB) dysfunction is central to many neurodegenerative and neuroinflammatory diseases. Understanding how inflammatory stimuli affect BBB integrity is key to identifying therapeutic targets.

Methods: An in vitro BBB inflammation model was established using human brain microvascular endothelial cells (HBMECs) cultured on transwell inserts. Cells were treated with lipopolysaccharide (LPS), a cytokine cocktail (TNF-α, IL-1α, C1q), and both. Assays measured cell viability (Crystal Violet), permeability (FITC-Dextran), and gene expression (qPCR) of tight junction markers (Claudin-5, Occludin, ZO-1) and inflammatory genes (IL-6, MCP-1, VCAM).

Results: Viability remained stable across conditions. Permeability increased significantly with LPS+Cytokines. Claudin-5 was upregulated under LPS+Cytokines; MCP-1 increased under cytokines. IL-6 showed a significant overall effect, though pairwise comparisons were non-significant. VCAM expression trended toward significance. Occludin and ZO-1 levels were unchanged.

Conclusion: The model reveals selective gene expression and increased permeability under inflammatory stress, validating it as a tool for studying BBB disruption and screening therapeutic strategies.

Topics: Neuroinflammation, Blood-Brain-Barrier, In Vitro Model

The anti-inflammatory and immunomodulatory potential of *Lactobacillus* synthesised EPS in macrophage

Megan Smith

Lactobacillus are a type of lactic acid bacteria capable of synthesizing exopolysaccharides (EPS) during fermentation. EPS are considered a functional food valuable to humans due to health benefits like immunomodulation. We examined the possible anti-inflammatory benefits of EPS samples to control chronic inflammatory diseases. We grew three Lactobacillus strains in MRS media: Lactobacillus delbrueckii subsp. bulgaricus 327 (LB 327), Lentilactobacillus kefiri 13 (LKF13) and Lacticaseibacillus rhamnosus 28 (LRH28). EPS was then isolated from each strain and lyophilised for analysis. We tested EPS samples for immunomodulatory potential using in vitro models of inflammation. We measured cytokine and chemokine secretion in J774A.1 murine macrophage cell line and assessed cell viability. Results show EPS samples had no effect on cell viability, decreased inflammatory cytokines IL-1β and TNF-α, increased anti-inflammatory IL-10, and had little effect on chemokine secretion in the presence of inflammatory stimulus lipopolysaccharide.

Results show EPS samples had anti-inflammatory effects in macrophage by reducing levels of pro-inflammatory cytokines, enhancing anti-inflammatory cytokines, maintaining chemokine secretion. This shows the ability of EPS samples as novel functional foods that can regulate immune responses by anti-inflammatory properties. We suggest a possible therapeutic effect for EPS in chronic inflammatory diseases like ulcerative colitis and Crohn's disease.

Topics: Anti-inflammatory, immunomodulatory, functional foods

Development of a functional precision oncology test to identify individual patients' response to therapy

Karla Jenkac

HER2+ breast cancer is characterised by the overexpression or amplification of the HER2/ERBB2 gene, affecting responses to treatment. Although HER2 amplification is known as a significant predictor of the effectiveness of targeted therapies, the influence of centromeric alterations on drug sensitivity has not been thoroughly researched.

This study combined in silico drug response data with in vitro cytotoxicity assays carried out on BT474, HCC1954, and SKBR3 HER2+ breast cancer cell lines. Gene expression was analysed through qPCR, focusing on the expression stability of candidate control genes from centromere adjacent regions of chromosomes 4, 7, 11, 17, and 19. The expression of HER2 and centromeric activity of chromosome 17 satellite (Censat_17_25) were assessed and correlated with drug sensitivity.

A strong correlation was observed between HER2 gene expression and drug sensitivity to taxanes and topoisomerase inhibitors, with the HCC1954 cell line showing greatest sensitivity, while BT474 demonstrated the highest resistance. The expression of Censat_17_25 varied between cell lines, indicating possible amplification. The expression of candidate control genes remained relatively stable, suggesting their potential as reference genes.

The levels of HER2 expression, centromeric amplification, and chemotherapeutic drug response are closely related. These results highlight the potential of centromeric regions as biomarkers and predictors of treatment response.

Topics: HER2+ breast cancer, Drug sensitivity and chemotherapy response, Centromeric amplification and copy number variation, Precision oncology

Unveiling the roles of non-coding mutations in breast cancer

Temi Akinbola

Breast cancer (BC) remains a leading cause of cancer-related mortality, with the PI3K/AKT signaling pathway frequently dysregulated in aggressive subtypes. While protein-coding mutations in PIK3CA and AKT1 have been well characterised, the role of noncoding mutations in AKT2 remains largely unexplored.

This project investigates whether a six-base-pair insertion at chr19:39858852 affects AKT2 expression. A luciferase reporter assay showed a 1.4-fold increase in promoter activity; However, the result was not statistically significant ($p = 0.136$). Despite this, the trend suggests the mutation may have a regulatory effect on AKT2. Given that AKT2 overexpression has been implicated in metastasis, therapy resistance, and poor prognosis, further studies are needed to determine if this mutation has clinical relevance.

Future studies will investigate the overexpression of AKT2 using plasmid-based systems or CRISPR-Cas9 methodologies to ascertain its functional relevance. Elucidating the mechanisms by which non-coding mutations cause AKT2 dysregulation can identify novel therapeutic targets for overcoming resistance in breast cancer.

Topic: Noncoding Mutations in Breast Cancer, Gene Expression and Oncogenesis, Metastasis and Therapy Resistance

The Impact of Cigarette Derived Pollutants on Daphnia magna

Sean Brennan & Reidin Myler

Cigarette pollution poses a significant threat to aquatic ecosystems and the broader environment. Cigarette butts are discarded improperly around the world, leaching toxic chemicals into our oceans, potentially causing severe harm to marine life and contributing to the decline in water quality. This study investigated the toxicological effects of smoked cigarette filter (SCF) leachate and rolling tobacco on Daphnia magna. A toxicity assay was conducted for each pollutant to generate a Hill model dose-response curve (% mortality) and determine effective concentration (EC) values. A seven-day growth assay assessed the impact of these pollutants on Daphnia magna development compared to an unexposed control. To evaluate physiological biomarkers, a biochemical assay measured the activity of five key enzymes: β-galactosidase, lipase, aminopeptidase, acid phosphatase, and alkaline phosphatase, where significant differences were observed after exposure to both SCFs and rolling tobacco. Additionally, Kaplan-Meier survival curves were used to visualise the time of death of daphnids upon exposure.

These findings provide a comprehensive understanding of the effects of cigarette-derived pollutants on Daphnia magna, highlighting their potential ecological consequences.

Topics: The impact of cigarette-derived pollution on aquatic ecosystems, Toxicological effects of cigarette filter leachate and rolling tobacco, Dose-response analysis using the Hill model in Daphnia magna

Development of ERBB3 gene mutation in breast cancer line using CRISPR/Cas9 gene editing

Jane Herlihy

In 2013, Bose et al. (Bose et al., 2013) published research into HER2 mutations in HER2- breast cancer, which remains one of the few studies completed on mutations in HER2- cancer. This project focused on introducing the V104L HER3 mutation to the breast cancer cell lines ZR7-51 (ER+/HER2-), CAMA1 (ER+/HER2-) and HDQ-P1 (ER-/HER2-) using CRISPR-Cas9 gene editing to examine their phenotypes. As breast cancer cells are notoriously difficult to transfect, we optimised stable and transient transfection methods to establish cell lines with increased expression of the Cas9 gene to increase retention of the V104L HER3 mutation. We collected results for two of the completed stable transfections, which had aimed to introduce the Cas9 gene to the ZR7-51 and CAMA1 lines, which yielded negative results. When we attempted to ligate the sequence for the V104L mutation into a Cas9 plasmid for the transient transfection, we found that we were unable to transform the ligated plasmid into the recombinant Stbl3 bacteria.

Through troubleshooting, we were able to eliminate issues with the digestion or ligation step, and troubleshooting with the transformation step is ongoing. We were able to optimise both of the processes by evaluating the reagents/concentrations used in them.

Topics: Breast cancer, gene editing, HER protein mutations, transfection optimisation

Evaluating the Predictive Accuracy of Detection Methods for Molecular Signatures in Uveal Melanoma

Katie Hanratty

Uveal melanoma is the most common intraocular malignancy worldwide, with consistently high rates of metastasis. The prognosis of patients is predicted using three biomarkers: BAP1 expression loss, monosomy 3, and chromosome 8q gain. The presence of these biomarkers helps clinicians stratify patients for more frequent surveillance for metastatic disease.

However, the current clinical methods used to detect these biomarkers—immunohistochemical (IHC) studies and fluorescence in situ hybridisation (FISH) studies—each have limitations.

The aim of this study was to perform whole-exome sequencing (WES) analysis on a cohort of patients to:

1. Predict BAP1 expression loss through somatic variant calling.

2. Detect monosomy 3 and chromosome 8q gain using copy number variant (CNV) calling algorithms.

3. Correlate the WES results with the FISH/IHC findings.

The results showed that WES-based CNV calls were largely concordant with FISH results, with some exceptions where sequencing outperformed FISH and vice versa. BAP1 expression loss was associated with large deletions or frameshift variants leading to premature stop codons both in the catalytic domain of BAP1. Cases with IHC-detected BAP1 expression carried either no variants or non-coding variants, with the exception of one missense variant detected.

To conclude, using WES analysis in conjunction with FISH/IHC could increase the predictive power and provide more insightful prognostic evaluation for patients in clinical settings.

Topics: Uveal Melanoma; Prognostic Biomarkers; BAP1; Copy Number Variant; Whole Exome Sequencing