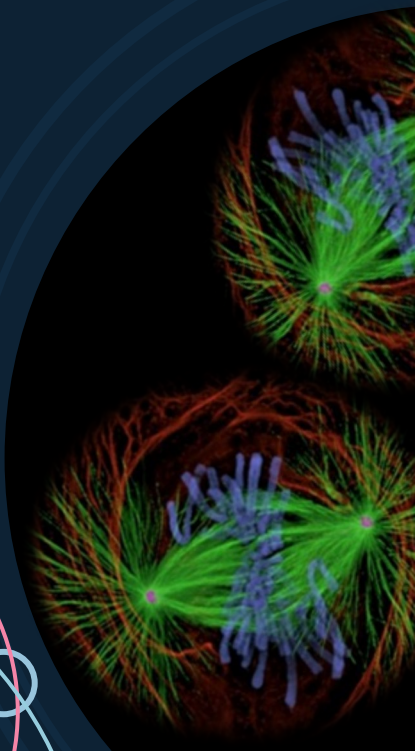
ICR The Institute of Cancer Research

Centre for Genome Stability Conference 2026



Welcome

On behalf of my fellow co-organisers, I am delighted to welcome you to the Centre for Genome Stability Conference, which brings together researchers and clinicians to explore the mechanisms underlying genome instability in cancer. We will hear the latest findings from research on DNA damage and repair to replication stress, chromosomal instability, and tumour evolution, that shed light on how genome stability can be disrupted, providing insights into how cancers develop, and revealing new opportunities for therapeutic intervention.

We are grateful to our invited speakers for giving us their time and expertise; I look forward to hearing from them, and from our colleagues across the Institute of Cancer Research and The Royal Marsden who will showcase the outstanding research taking place across the Centre.

I hope this conference will foster stimulating scientific discussions, encourage the exchange of ideas, and inspire new collaborations across disciplines. My sincere thanks to all our speakers and to you all for contributing to this meeting, and I wish everyone an engaging, productive, and above all, enjoyable conference.



Professor Jonathon Pines FRS

Chris Marshall Chair of Cell Biology
Head, Division of Cell and Molecular Biology

CENTRE FOR GENOME STABILITY

Programme

Monday 26 October	
0930	Welcome: Professor Jon Pines
	Chair: Professor Jessica Downs
0945	Professor Geert Kops
1015	Professor Serena Nik-Zainal
1045	Break
1115	Professor Keith Caldecott
1145	Dr Vivianne Lebrec
1215	Antibody Facility: Dr Divya Duscharla
1235	Lunch
	Chair: Professor Sebastian Nijman
1400	Dr Syed Haider
1430	Dr Sheena Guram
1500	Break
1530	Professor Jessica Downs
1600	Dr George Seed
1630	Dr Jörg Mansfeld

Tuesday 27 October	
	Chair: Professor Chris Lord
0930	Dr Helen Robinson
1000	Dr Claudio Alfieri
1030	Break
1100	Professor Petr Cejka
1130	Dr Navita Somaiah
1200	Professor Trevor Graham
1230	Lunch
	Chair: Prof Wojciech Niedzwiedz
1400	Professor Jesus Gil
1430	Dr Khushoo Agrawal
1500	Break
1530	Professor Chris Lord
1600	Dr Jadwiga Nieminuszczy
1630	Closing remarks: Prof Jon Pines

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Talk Abstracts



Professor Geert Kops

Chromosomal instability, p53 activity, and karyotype evolution in cancer

Most cancer types are marked by signature chromosomal copy number alterations. It is thought that these arise by a combination of 1) chromosomal instability; 2) adaptation to aneuploidy-related stresses, for example by p53 inactivation; and 3) selection for tissue-specific fitness benefits from particular chromosomal copy number states. I will discuss our efforts, using cancer genomes and transcriptomes, single cell sequencing, live imaging, and in vitro evolution of cell lines and colonic precancer organoids to assess the roles of chromosomal instability and p53 inactivation in the emergence of signature karyotypes.



Professor Serena Nik-Zainal

DNA Repair Deficiency Through the Lens of Cancer Genomes: Mechanism and Evolution

Cancer genomes retain a cumulative record of the biological processes that have operated throughout tumour development. Among the most striking examples are the characteristic patterns of mutation associated with defects in DNA repair, which can provide insights into both the mechanisms generating genomic instability and their consequences for tumour evolution.

Whole-genome sequencing enables these processes to be examined across multiple classes of genomic variation, including substitutions, insertions and deletions, and structural rearrangements. Using homologous recombination deficiency as an established paradigm, I will illustrate how combinations of mutational patterns can identify underlying repair defects, inform mechanistic studies and ultimately generate clinically useful biomarkers. I will then discuss how genomic observations can reveal less well-characterised forms of DNA repair dysfunction, including defective ribonucleotide excision repair, and how experimental systems can be used to establish the mechanisms responsible for these patterns.

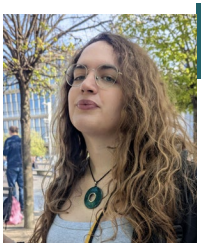
Finally, I will consider how genomic features acquired during tumour development can provide insight into cancer evolution and aggressive disease. Together, these studies illustrate how cancer genomes can be read not simply as catalogues of mutations, but as dynamic historical records connecting DNA repair mechanisms, tumour evolution and clinical phenotype.



Professor Keith Caldecott

PARP activity in DNA repair and replication

DNA single-strand breaks are amongst the commonest lesions arising in DNA, resulting not only from attack by endogenous and environmental genotoxins but also from enzymatic errors occurring during normal DNA metabolic processes such as DNA replication and gene transcription. The threat posed by SSBs is illustrated by the existence of human genetic diseases in which genes/proteins involved in single-strand break repair are mutated. Here, I will discuss our work aimed at understanding how single-strand breaks are detected and repaired in human cells, with a focus on their detection by PARP enzymes and their relevance to DNA replication and cancer.



Dr Vivianne Lebrec

Mechanisms of cGAS activation from DNA damage and chromosome instability

Cyclic GMP-AMP synthase (cGAS) is the main innate immune sensor driving inflammation in response to DNA viruses. Upon binding to DNA, cGAS generates the second messenger cGAMP, activating STING and ultimately driving inflammation. Activation from nuclear self-DNA is inhibited by chromatin, yet it has been shown that following DNA damage, cGAS can be activated, although the underlying mechanisms have remained speculative due to a lack of sensitive and selective single-cell cGAS activation assays.

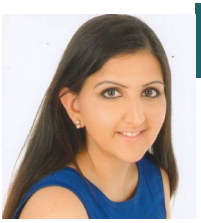
To tackle these questions, we recently developed a FRET-based reporter to directly assess cGAS activity in microscopy, flow cytometry and biochemical assays. Strikingly, we found that following a large variety of genotoxic treatments, only a small minority of cells activate cGAS, and that this activation is not driven by micronuclei, contrary to a popular hypothesis in the field. In contrast, we found that cGAS active cells are frequently associated to chromatin bridges, although only following certain types of genotoxic stress, therefore arguing against a single unifying mechanism. Together with these findings, I will present our current progress in identifying the cellular events and molecular processes promoting cGAS immunostimulation following genotoxic stress.



Dr Syed Haider

In-silico approaches to identifying new synthetic lethal target genes

One of the key challenges in cancer drug discovery is finding targets that cancer cells need to survive, but that healthy cells can live without. Our research addresses this challenge by developing new in-silico ways to identify and prioritise cancer drug targets through the large-scale integration of patient data, human genetics and functional genomics. Building on the principles of BRCA1/2-PARP1 synthetic lethality, we use patient-derived molecular and clinical data to identify higher-order synthetic lethal vulnerabilities associated with specific tumour subtypes. We then investigate the underlying biology and develop experimental strategies to establish whether these vulnerabilities can be therapeutically exploited.



Dr Sheena Guram

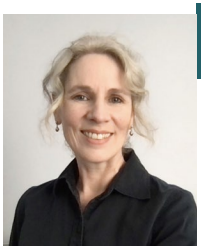
Targeting Replication Stress in Fusion Driven Sarcomas of Childhood

Fusion Positive RhabdoMyoSarcoma (FP-RMS), Ewing Sarcoma (ES) and Desmoplastic Small Round Cell Tumours (DSRCT) are aggressive sarcomas of childhood and adolescence and remain major causes of cancer-related mortality in these age groups. Despite the use of multi-modal therapy, local failure after radiotherapy remains a significant clinical challenge. These tumours are driven by pathognomonic fusion proteins; PAX3/7::FOXO1 in RMS, EWSR1::FLI1 in ES and EWSR1::WT1 in DSRCT which act as unique transcription factors that potently drive tumour initiation and progression. Increasing evidence suggests that these fusions induce replication stress (RS) and genomic instability, creating a dependence on the replication stress response (RSR) pathway. Here, the vulnerability of targeting the RSR with ATR inhibition to sensitise to RT is assessed for therapeutic translation.

Three-dimensional spheroid models from FP-RMS cell lines (RH4, RH41 & RH30) and a PDX-derived cell line (ICR_PDX_RMS006) were used to evaluate three ATR inhibitors (AZD6738, VX970, BAY1895344) and RT. Spheroid growth, viability and mechanistic effects were assessed using longitudinal measurements, CellTiter-Glo® assays and immunofluorescence. *In vivo* testing was conducted using an athymic nude mouse xenograft model of RMS. Mice received vehicle, AZD6738 (75 mg/kg daily), RT (5 × 2 Gy RH4/RH30; 3 × 2 Gy ICR_PDX_RMS006) or combination. Efficacy was assessed using calliper measurement of tumour growth and circulating tumour DNA (ctDNA) extracted from serial vein tail blood samples.

Combined ATRi and RT significantly reduced spheroid growth in all xenograft models. Increased DNA damage and apoptosis was evidenced by increased gamma H2AX foci and cleaved caspase 3 by

immunofluorescence. In vivo, combined AZD6738 and RT improved tumour control and delayed progression compared with monotherapies in all xenograft models ($p < 0.0001$). This was consistent with findings from exploratory assessment of ctDNA as a potential minimally invasive biomarker of response.
ATR inhibition enhances RT control of FP-RMS xenograft tumours through increased DNA damage and apoptosis. This supports the RSR as a targetable therapeutic vulnerability and provides strong rationale for clinical evaluation of ATR inhibition as a radio-sensitisation strategy for FP-RMS.



Professor Jessica Downs

Functional profiling of SWI/SNF chromatin remodelling complexes through base editing screens

Mammalian cells contain multiple SWI/SNF chromatin remodelling complexes, termed BAF, PBAF, and ncBAF. These contribute to multiple cellular activities, including gene expression, DNA replication stress responses, and DNA repair. Genes encoding subunits of the SWI/SNF chromatin remodelling complexes are frequently misregulated in cancer, and loss of function studies demonstrate a role in preventing tumourigenesis. However, the functional significance of a great number of clinically observed mutations in SWI/SNF genes is unclear. Here, using a base editing approach in two cell line models, we systematically investigate the contribution of individual amino acids across the entire SWI/SNF gene repertoire to cellular fitness. Through this approach, we identify patterns of functionally important domains and motifs and compare these to alterations identified in patient datasets across different tissues and cancer types. Furthermore, we identified novel motifs that mediate interaction with DNA structures and promote genome stability. These data shed light on the pattern and functional significance of cancer-associated alterations of SWI/SNF subunits.



Dr George Seed

Genome Instability in HPV+ Head and Neck Cancers

Around half of Oropharyngeal Head and Neck Squamous Cell Carcinomas (OPSCC) are defined by the presence of the human papillomavirus (HPV), which initiates oncogenesis by inhibiting RB and p53, promoting unchecked growth and genomic instability.

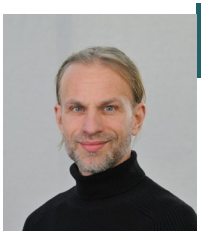
Clinical classification remains limited to immunohistochemistry, with no genomic biomarkers defining different treatment options. To address this, we pursued deep targeted viral sequencing alongside matched low-pass whole-genome sequencing and RNA-seq of a cohort of HPV+ HNSCC tumours (n=180) to jointly interrogate the underlying structure

of the HPV genome and identify human-viral DNA integration events alongside conventional copy-number and expression profiling.

Almost half (~45%) of the studied cases bore multiple sub-clonal (>2) human-viral structural breakpoints, alongside elevated (>10) viral copy numbers, while 'classical' single-breakpoint cases accounted for a minority (~15%) of the cohort. Further, ~20% of all cases exhibited no evidence of viral integration despite ultra-deep sequencing and high viral copy numbers (median CN = 100).

In ongoing work we explore these genomic architectures using multi-region sequencing, identifying independent sub-clonal integrations between different areas of the same tumour, and show that under treatment pressure these can be clonally selected.

Our findings show that integration alone is not the necessary endpoint of HPV+ HNSSC, and that underlying genomic instability supports a huge richness in sub-clonal viral structural variants.



Dr Jörg Mansfeld

How Reactive Oxygen Species Dictate Cell Fate: From Mechanisms to Medicine

Reactive oxygen species (ROS) have long been viewed primarily as harmful products of metabolism and environmental exposure, causing oxidative damage to proteins, DNA and lipids and contributing to genome instability. Yet, at the right levels and locations, ROS also act as signalling molecules. Through reversible oxidation of specific cysteine residues, they can regulate protein activity, stability and localisation, thereby controlling cellular processes, including proliferation. In cancer cells, metabolism and redox homeostasis are frequently dysregulated, and elevated ROS levels can support tumourigenesis. However, the molecular mechanisms connecting these redox changes to the machinery governing cell proliferation remain incompletely understood.

Our laboratory investigates how ROS influence proliferation and cell fate and develops tools to detect and manipulate ROS with spatial and temporal precision. We are establishing highly sensitive mass-spectrometry-based redox proteomics approaches, including methods tailored to patient material, to identify oxidised proteins and uncover regulators of the decision to proliferate or exit the cell cycle. By combining these approaches with functional studies, we aim to define redox-dependent mechanisms of cell-cycle control and identify opportunities for clinical translation. I will discuss two complementary mechanisms we have identified involving cyclin-dependent kinase 2 (CDK2), a key driver of cell-cycle progression, and its inhibitor p21. Oxidation of a single cysteine residue in CDK2 sustains its activity and

promotes DNA replication, whereas oxidation of a cysteine residue in p21 promotes its turnover. Together, these mechanisms reveal how ROS can favour proliferation by acting on both a cell-cycle driver and its inhibitor. They also demonstrate how protein oxidation can influence the choice between continued proliferation and cell-cycle exit, including senescence following irradiation. Given the importance of CDK2 and p21 in cancer, these findings suggest that their oxidation states may contribute to sustained tumour cell proliferation and offer potential entry points for therapeutic intervention.

We are extending this work to breast cancer patient samples in collaboration with clinician-scientist Dr Navita Somaiah, Chief Investigator of the phase II KORTUC trial at The Institute of Cancer Research (ICR). The trial tests whether intratumoural hydrogen peroxide injections improve the effectiveness of radiotherapy. By identifying and functionally characterising treatment-associated changes in protein oxidation in these samples, we aim to link molecular redox mechanisms to treatment responses and explore the potential of redox proteomics for biomarker discovery and diagnostics.



Dr Helen Robinson

Combination of ATR inhibition with low dose irinotecan is efficacious in ATM deficient cancers

Ataxia telangiectasia mutated (ATM) and Ataxia telangiectasia and Rad3-related (ATR) proteins function in concert to regulate the cellular response to both intrinsic and extrinsic factors that induce replication stress such as oncogene activation and DNA damaging agents. Loss or inhibition of ATR has been well documented to be synthetic lethal with ATM deficiency in cancers and this concept has been explored in clinical trials, however, the efficacy of ATR inhibition as monotherapy in this setting has been limited, with objective response rates of ~10%. Here, using a novel ATR kinase inhibitor, alnodesertib (ART0380), we provide mechanistic preclinical evidence across a range of *in vitro* and *in vivo* models, that exacerbating replication stress with a low dose of the TOP1 inhibitor, irinotecan, further sensitises ATM negative tumors to ATR inhibition. We also provide early clinical evidence of meaningful activity of this combination in a Phase I/IIa study (NCT04657068)[1].

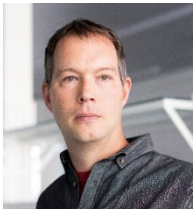
[1]Ulahannan et al. Cancer Res (2025) 85 (8_Supplement_2): CT267



Dr Claudio Alfieri

Catching the DREAM: Cryo-EM Insights into Cell Cycle Regulation by the MuvB/DREAM complexes

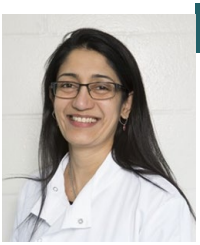
The cell cycle is the fundamental biological process where the cell coordinates chromosome replication and segregation with cell growth and division. Cell cycle exit controls cell proliferation and is crucial for development, tissue regeneration, and tumour biology. Cell cycle progression is promoted by the cyclins, which activate the cyclin-dependent kinases and are regulated at the transcriptional level. A key regulator of cellular proliferation and cell cycle exit is the MuvB complex, a bifunctional transcriptional regulator which represses cyclin genes during cell cycle exit (i.e.DREAM complex), and switches to an activator during cell proliferation. Although the MuvB pathway is crucial for controlling cell proliferation and its dual function in transcription is intriguing, we do not know how these processes work at the molecular level. To increase our knowledge into the latter, we aim to investigate (i) the mechanism(s) of transcriptional regulation by the MuvB complexes (ii) the interplay between MuvB and its associated factors/enzymes (iii) the MuvB switch from repressor to an activator. This will propel our understanding of how a dual function transcriptional regulator can switch from a repressor to an activator to control cellular proliferation, thereby gaining insights into how cell cycle dependant transcription fine tune the cell cycle.



Professor Petr Cejka

Understanding mechanisms of trinucleotide repeat instability through biochemical reconstitution

Trinucleotide repeat expansion underlies numerous human disorders. Genome-wide association studies using patient data, as well as animal and cellular models, have identified modifiers of repeat instability; however, the mechanisms underlying this process have remained unclear. We have established biochemical systems that reconstitute key elements of both repeat expansion and repeat contraction. These reactions, performed with purified recombinant proteins, provide mechanistic insight into the molecular processes driving repeat instability. They can also serve as the basis for screening compounds that target the enzymes involved. I will present our recent advances in our understanding of trinucleotide repeat instability driven by MutSbeta, MutLbeta and MutLgamma.



Dr Navita Somaiah

Modulating Redox Biology to Improve Radiation Responses

Redox biology plays an important role in cancer progression and therapy resistance. Tumour cells maintain elevated levels of reactive oxygen species (ROS) to support proliferation while upregulating antioxidant defences to avoid oxidative cell death. Radiotherapy, a standard treatment for over half of all cancer patients, relies on the generation of ROS and adequate oxygen availability for efficacy. However, hypoxic tumour microenvironments and enhanced antioxidant systems contribute significantly to radioresistance. This redox imbalance, which is characteristic of tumour cells, presents a therapeutic opportunity where modifying redox biology may sensitise tumours to radiation and promote cell death.

One such treatment is KORTUC, a mixture of 0.5% H_2O_2 in sodium hyaluronate gel, administered via intratumoural injection. Our Phase 1 trial (PMID 32585332) has confirmed safety, and we have just completed recruitment to the first randomised Phase 2 trial (NCT03946202) testing efficacy in locally advanced breast cancer. However, the mechanisms of action of intratumoural H_2O_2 and its effects on intracellular redox balance and cell death is not yet fully understood.

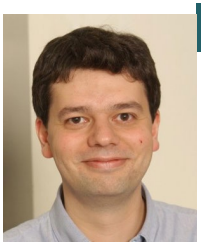
ROS induced post-translational modification of proteins at cysteine residues (Cys) containing thiol (-SH) groups can be reversible and confer functional changes, as with redox switches, or permanently alter proteins leading to dysfunction in cellular metabolism. We are characterising the effects of intratumoural H_2O_2 on ROS-mediated pathways in preclinical models, including effects on the redox proteome via cysteine oxidation, and exploring opportunities for combination therapy with other agents that may enhance radiosensitisation. In collaboration with the Mansfeld and Choudhary labs we are testing a new data-independent approach in mass spectrometry proteomics, paving the way for a more time- and cost-effective analysis, requiring smaller protein yields that can be readily translated to analysis of patient samples.



Professor Trevor Graham

Single cell resolution of genome and epigenome coevolution in colorectal cancer

Genetic mutations and epigenetic alterations are intertwined because mutations can precipitate epigenetic remodelling, and the state of the epigenome defines the genetic mutation rate. Further, both genetic and epigenetic alterations are heritable and so can directly drive cancer evolution. In this talk I will describe our development of a new single cell sequencing method called “dATAC” that enables simultaneous whole genome sequencing (WGS) and chromatin accessibility profiling (ATACseq), enabling lineage-tracing of epigenome alterations through cancer evolution by using somatic mutations as endogenous clonal markers. We performed dATAC sequencing of ~50,000 colorectal cancer cells to map genome-epigenome coevolution in metastatic disease and through treatment in model systems. Initial results show: (1) epigenome remodelling occurs convergently in independent clonal lineages, (2) copy number alterations rarely precipitate epigenome remodelling, (3) the chromatin state strongly determines the SNV mutation rate.



Professor Jesus Gil

Cellular senescence as a therapeutic target

Senescent cells are present in cancerous and fibrotic tissues and are associated with multiple age-related diseases. Recently, drugs that selectively kill senescent cells, termed senolytics, have proven beneficial in improving the outcomes of many of these pathologies, including cancer. While the potential of senotherapies is great, there are several limitations to translating them to the clinic. In particular, we need to better understand the complex biology of senescence, identify effective senolytics, and develop ways to detect senescent cells. I will describe functional approaches that my lab has employed to identify senotherapies and how we can take advantage of machine learning to detect senescence.



Dr Khushboo Agrawal

NF1 loss disrupts a SMARCA2–CTCF–H1 chromatin-remodelling axis and creates DNA repair vulnerability in retinoic acid–resistant high-risk neuroblastoma

Neuroblastoma (NB) is an aggressive childhood malignancy arising from the developing sympathetic nervous system. *NF1* loss-of-function (LoF) and activating-*RAS* mutations both result in downstream activation of RAS-pathway signalling, are enriched at relapse, and associated with differentiation block.

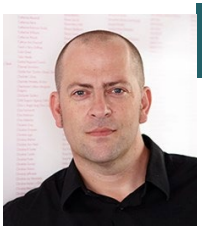
We show that failure to downregulate RAS-MEK-ERK signalling in both *NF1* mutant and *RAS* mutant NB cells is associated with resistance to the standard of care differentiation therapy: retinoic acid (RA). Given the

role of SWI/SNF and PRC2 chromatin-remodelling complexes in RA-mediated differentiation, we predicted SWI/SNF, PRC2, and RAS pathway functional interactors, using publicly available datasets and then evaluated RNA and protein expression of these key interactors across large panel of NB cell lines. These included patient-derived *NF1* wild-type and *NF1* mutant cell lines, CRISPR–Cas9-generated *NF1*-knockout cells and an inducible $NRAS^{Q61K}$ overexpression model. We identified consistent downregulation of the SWI/SNF ATPase subunit SMARCA2 at both transcriptomic and proteomic levels across all *NF1*-deficient models. However, SMARCA2 expression remained unchanged following induction of $NRAS^{Q61K}$ expression. *NF1*-knockout cells were then treated with the MEK inhibitors (MEKi) trametinib and cobimetinib to suppress downstream phospho-ERK, but this failed to restore SMARCA2 expression. Taken together this identifies that although RA resistance is a common phenotype of oncogenic RAS-pathway signalling in NB, SMARCA2 downregulation is specific to *NF1* LoF and occurs via a mechanism that is independent of canonical RAS–MEK–ERK signalling.

We then evaluated the chromatin bound proteome by mass spectrometry in 1. matched *NF1* wild-type and knock-out cells and 2. matched *RAS* wild-type and $NRAS^{Q61K}$ expressing cells. This confirmed *NF1* loss–specific downregulation of SMARCA2 on chromatin. *NF1* knock-out cells also showed significant down-regulation of chromatin bound DNA replication and repair machinery proteins in addition to loss of CTCF and linker histone H1 variants. Immunoprecipitation for the core SWI/SNF subunit SMARCC2 confirmed reduced enrichment of CTCF and H1 proteins, together with SMARCA2 loss, in *NF1*-knockout cells. These findings support disruption of a SMARCA2–CTCF–H1 chromatin architecture axis in *NF1* mutant NB.

Given our findings, we hypothesised that the combination of PARPi and MEKi would be synergistic in *NF1*-deficient NB. *In vitro* drug synergy studies revealed the combination of the PARPi niraparib and the MEKi cobimetinib to be highly synergistic in *NF1*-mutant, but not *NF1* wild-type or $NRAS^{Q61K}$ overexpression models. *In-vivo* studies are ongoing.

In summary, we identify *NF1* loss–specific chromatin-remodelling resulting in impaired DNA-damage repair and show that PARP–MEKi combinations are a potential therapeutic strategy for *NF1* mutant high-risk NB. This study addresses a critical unmet need in *NF1*-mutant high-risk NB, particularly at relapse or progression, where treatment options are limited. (supported by ICR HEFCE and CRUK CSF).



Professor Chris Lord

How does genomic stability influence the treatment of BRCA1/2 mutant cancers

Although PARP inhibitors have transformed the treatment of BRCA1 and BRCA2 mutant cancers, their overall effectiveness is blunted by drug resistance, often caused by reversion mutations in either tumour suppressor gene. I will describe how BRCA1/2 reversions are a dominant cause of resistance and how by studying clinically occurring reversions identifies the domains of BRCA1 and BRCA2 which are essential for resistance. This information allows those patients most likely to later develop resistance via reversion to be identified, a population who could, in principle, benefit from more treatment and/or additional monitoring whilst on treatment. I will also describe how efforts to suppress reversion formation via inhibition of microhomology mediated end joining do not prevent reversions but simply alters their sequence context as well as showing that reversions in mice can be targeted by the design of vaccination strategies that exploit the antigenic nature of these newly evolved mutations.



Dr Jadwiga Nieminuszczy

DTX3L-dependent ubiquitylation of 3' DNA ends couples replication fork protection to homologous recombination

Stalled replication forks must be stabilised and restarted without generating aberrant recombination intermediates, and failure of this process drives chromosomal instability. Here we identify the E3 ubiquitin ligase DTX3L as a regulator of replication fork protection and homologous recombination.

DTX3L is recruited to perturbed replication forks, and full-length DTX3L binds replication-fork-like substrates *in vitro*. Loss of DTX3L causes increased fork stalling, impaired fork restart, pathological degradation of nascent DNA and accumulation of S1 nuclease-sensitive ssDNA gaps. These defects are accompanied by elevated 53BP1 nuclear bodies, micronuclei and anaphase bridges. DTX3L loss also markedly increases sister chromatid exchange (SCE); these SCEs require SLX4 and are further elevated by BLM depletion, indicating that DTX3L and BLM limit crossover-type resolution through non-epistatic mechanisms.
DTX3L has been shown to ubiquitylate the 3' termini of ssDNA and ssRNA *in vitro*. We show that 3'-terminal ubiquitylation protects DNA ends from exonucleolytic degradation and blocks their extension by DNA polymerases, providing a biochemical basis for the phenotypes observed in cells.

These data support a model in which DTX3L binds fork-associated DNA structures and modifies 3' ssDNA ends to couple protection of stalled forks to the control of homologous recombination, restraining crossover formation and genome instability.

Poster Presenters

Patrycja Domeracka

Michael Gruet

Will Kerrison

Hugh Selway-Clarke

Dragomir Krastev

Isabella Scott

Aarmann Mohan

Eetu Holtta

Emma Thorley

María Fernández-Casañas

Sonia Fanelli

Holly Sanderson