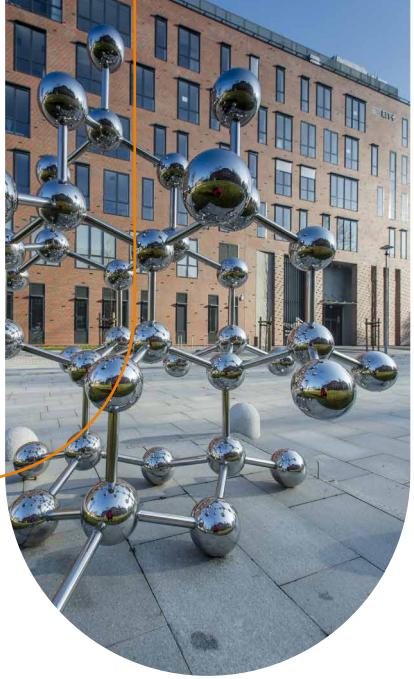
Łukasiewicz
PORT

PORT FOR
HEALTH
ONCOLOGY

PORT for Health: Oncology

28–30th September 2022

PORT for Health:
Oncology



PORT FOR HEALTH is an annual conference series, focused on life sciences, that brings together scientists, medical practitioners and industry professionals. Each year, the conference discusses a specific scientific topic that is important within the broad landscape of modern biomedical science and has strong implications for human health. There is an alternating biennial schedule focusing either on neuroscience or oncology. Themes discussed at the meeting include the fundamental molecular mechanisms, development of physiological models of human disease, finding of new drug targets and opportunities for novel targeted treatments in personalised medicine.

PORT FOR HEALTH is organised by the Life Science and Biotechnology Center located at the Łukasiewicz – PORT Polish Center for Technology Development, a part of the Łukasiewicz Research Network. The vision of the dynamically growing Life Science and Biotechnology Center at PORT is to tackle the biggest challenges of modern medicine through top-notch, translational research accomplished by teams led by creative and experienced leaders.

The oncology branch of the Center focuses on understanding of the molecular and cellular basis of cancer, one of the most significant health and socioeconomic problems of the current world. This year's conference will host top scientific leaders in oncology and will comprise a range of scientific sessions focusing on the biological basis of cancer, new treatment strategies as well as modalities and the latest achievements in tumor diagnostics.

The mission of the Conference is to foster interactions and knowledge exchange among scientists, clinicians and industry representatives leading to new ideas and inspiration for novel solutions in medical biotechnology.

Łukasiewicz
PORT
Polish Center
for Technology
Development

Łukasiewicz – PORT Polish Center for Technology Development is a research and development Institute. Our scientists conduct basic research and develop new technologies for industry.

The scientific and research activity of the Institute is based on three centers: Materials Science, Life Science & Biotechnology, and Population Diagnostics. Research Groups as well as specialized and measurement laboratories operate within these units.

The Life Science & Biotechnology Center is a modern institution with a research, development, and implementation profile. It focuses on significant current civilization problems and develops competencies in neurobiology, oncology, and biotechnology as broadly understood.

Łukasiewicz – PORT is located in the historic Pracze Campus. It consists of buildings erected at the turn of the 19th and 20th centuries, surrounded by greenery. Brick walls house modern laboratories with world-class equipment that enables the implementation of both application research projects and basic research.

Since 2019, our Institute is part of the Łukasiewicz Research Network, the third-largest research network in Europe. It connects 26 institutes from all over Poland, and its goal is to build a bridge between science and business.

Committee

Michał Malewicz, Ph.D.

Director of Life Science and Biotechnology Center

Michal's scientific work began at the University of Warsaw (Poland) where he defended a master's degree in molecular biology on the genetics of RNA metabolism in yeast mitochondria. Thereafter Michal moved to Karlsruhe Institute of Technology (Germany), where his Ph.D. thesis focused on the function of the immune system in genetically engineered mice. For his postdoctoral studies, Michal moved to Stockholm (Sweden) to work at the Ludwig Institute of Cancer Research (affiliated with the Nobel Karolinska Institute), where he developed new biochemical methods to study protein-protein interactions. In 2012 Michal was appointed as an Independent Group Leader at the MRC Toxicology Unit (United Kingdom) to build and run a scientific group working on mechanisms of DNA damage responses (DDR). In 2019 Michal moved back to Germany to work as the Head of Molecular Biology at an early-stage biotech Genome Biologics, where he had directed the team working on novel human heart organoid technology. From the end of 2020, Michal is directing the Laboratory of Genome Dynamics (Łukasiewicz – PORT, Poland), where his group focuses on the mechanisms of DNA damage responses and their connection to cancer development utilizing CRISPR/Base editing genome editing technologies and advanced models of disease such as iPSC-derived human organoids. From the beginning of 2022, Michal had been appointed as the Director of Life Science and Biotechnology Center at Łukasiewicz – PORT.

Patrycja Gazińska, Ph.D.

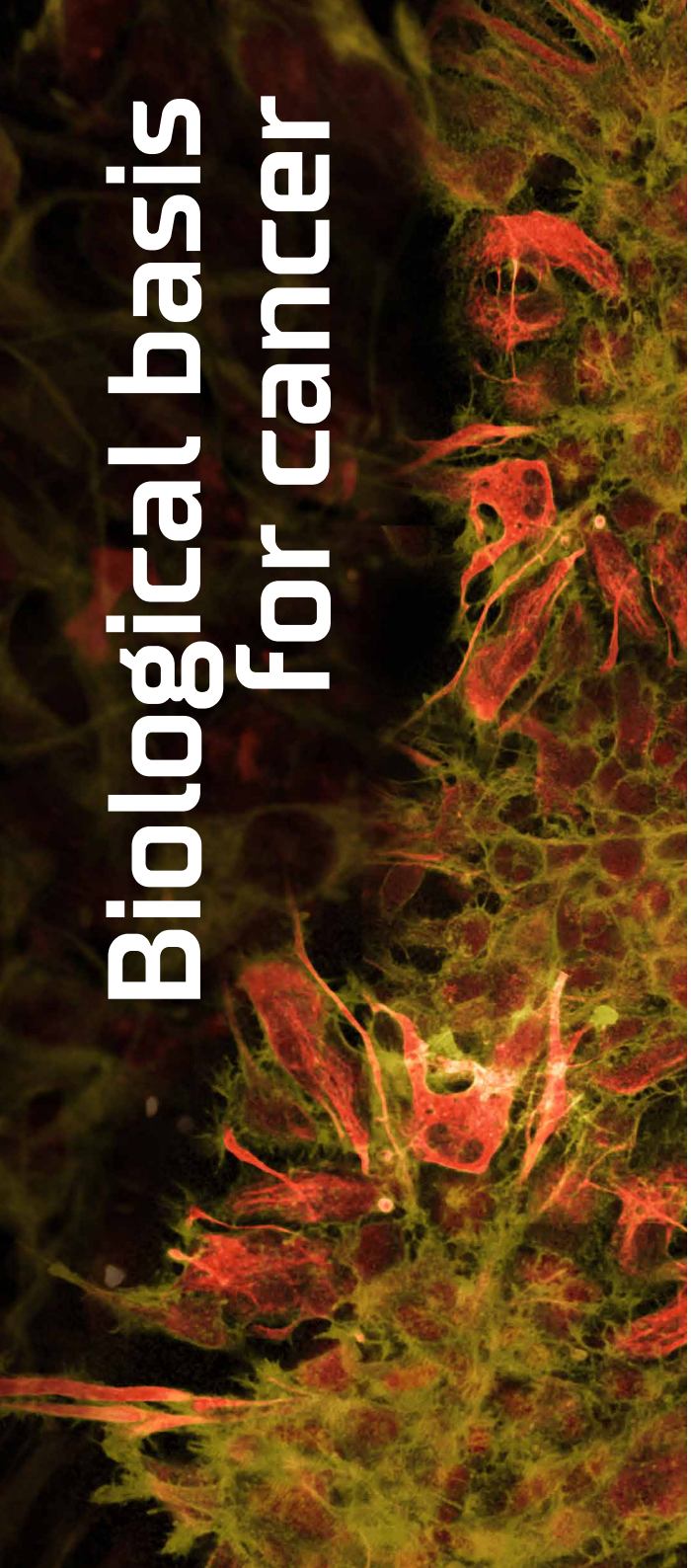
Senior Leader for the Biobank Research Team

She is the Senior Leader for the Biobank Research Team at Łukasiewicz – PORT Polish Center for Technology Development in Wroclaw. For many years, Patrycja managed histopathology research projects and services for multidisciplinary teams at Kings College in London. From 2019 to 2021, she led a Digital & Experimental Research Pathology unit at the Institute of Cancer Research in London specializing in digital pathology, and molecular pathology, with specific application to breast cancer research. This included collaborative work with Merck on novel biomarkers for patient treatment stratification. More recently she worked for AstraZeneca in Cambridge, applying computational pathology frameworks to oncology phase III clinical trials. Her primary research interest relates to breast cancer pathology and understanding how tumor microenvironment features predict clinical and biological aspects of this disease.

Grzegorz Chodaczek, Ph.D.

Head of Bioimaging Laboratory

He graduated from the Wroclaw Medical University in 2001, where he studied at the Faculty of Pharmacy. In 2007, he received his Ph.D. degree in immunology from the Institute of Immunology and Experimental Therapy in Wroclaw, Poland. Between 2005–2011 he was a research associate at the University of Texas Medical Branch at Galveston and then a postdoctoral fellow at the University of Texas MD Anderson Cancer Center in Houston, TX, in the Department of Immunology. His postdoctoral project involved intravital imaging of the immune system during wound healing and cancerogenesis. In 2011, he started a new position as microscopy core manager and instructor at La Jolla Institute for Immunology, San Diego, CA. Since 2014, he has worked as the Head of Bioimaging Laboratory at Łukasiewicz Research Network – PORT Polish Center for Technology Development. His research interest is in visualizing the immune cell activity in tissues, including the cancer microenvironment.



Merkel cell carcinoma (MCC) – an ultra-rare and highly aggressive skin cancer: unmet needs and challenges in 2022

Piotr Donizy

Wroclaw Medical University, Poland

Merkel cell carcinoma (MCC) is a rare and aggressive primary cutaneous neuroendocrine carcinoma with frequent recurrences, regional and distant metastases, high mortality rates, and rapidly increasing reported incidence. MCC pathogenesis is associated with the Merkel cell polyomavirus infection and chronic ultraviolet light (UV) exposure. MCC is a solitary, rapidly growing cutaneous or subcutaneous tumor, most frequently located in sun-exposed areas. Histopathologic examination is essential for the correct diagnosis and relies on specific morphologic features of tumoral cells and characteristic immunohistochemical profile. At the time of primary tumor diagnosis, metastases at regional lymph nodes are already present in 30% of patients. First-line therapy is a surgical excision; if not feasible radiotherapy could be used. There are very limited therapeutic options for the patients in advanced stage or refractory MCC.

Targeting transcriptional and signaling pathways in osteosarcoma pathogenesis and metastasis

Agi Grigoriadis

King's College London, UK

Osteosarcoma (OS) is a rare bone cancer and the most common primary malignancy of the skeleton, occurring primarily in children and adolescents. Metastatic disease is the single most important prognostic factor with a high frequency of patients developing lung metastases, resulting in low survival rates. We have generated the first OS mouse model where the c-Fos/AP-1 oncogene drives bone cell transformation and rapid tumour growth. Using a number of *in vitro* and *in vivo* xenograft approaches, we have demonstrated that high FGFR1 signalling contributes to the rapid tumour growth and metastasis of OS, and further, kinase screens demonstrated cooperation with mTOR signalling. Genetic silencing as well as small molecule combinatorial inhibition of both FGFR and mTOR signalling abrogated metastatic spread *in vivo*. Analysis of activated FGFR and mTOR pathways in patient-derived tissue microarrays will enable patient stratification that will be useful in the clinical setting to exploit this as a potential anti-metastatic therapy in OS.

Spatial genomics maps the structure, character and evolution of cancer clones

Lucy Yates

Wellcome Trust Sanger Institute, UK

Genome sequencing of cancers often reveals mosaics of different subclones present in the same tumour. While these are believed to arise according to the principles of somatic evolution, the exact spatial growth patterns and underlying mechanisms remain elusive. To address this need, we developed a workflow that generates detailed quantitative maps of genetic subclone composition across whole tumour sections. These provide the basis for studying clonal growth patterns, and each clone's histological characteristics, microanatomy, and microenvironmental composition. The approach rests on WGS, followed by highly multiplexed base specific in-situ sequencing (BaSISS), single cell resolved transcriptomics and dedicated algorithms to link these layers. Applying the BaSISS workflow to 8 tissue sections from two multifocal primary breast cancers, revealed intricate subclonal growth patterns that were validated by microdissection. In a case of ductal carcinoma in situ (DCIS), polyclonal neoplastic expansions occurred at macroscopic scale but segregated within microanatomical structures. Across the stages of DCIS, invasive cancer and lymph node metastasis, subclone territories are shown to exhibit distinct transcriptional and histological features and cellular microenvironments. These results provide examples of the benefits afforded by spatial genomics for deciphering the mechanisms underlying cancer evolution and microenvironmental ecology.

Exploring drivers phenotypic plasticity in pheochromocytoma, paraganglioma and neuroblastoma progression

Sussane Schlisio

Karolinska Institute, Sweden

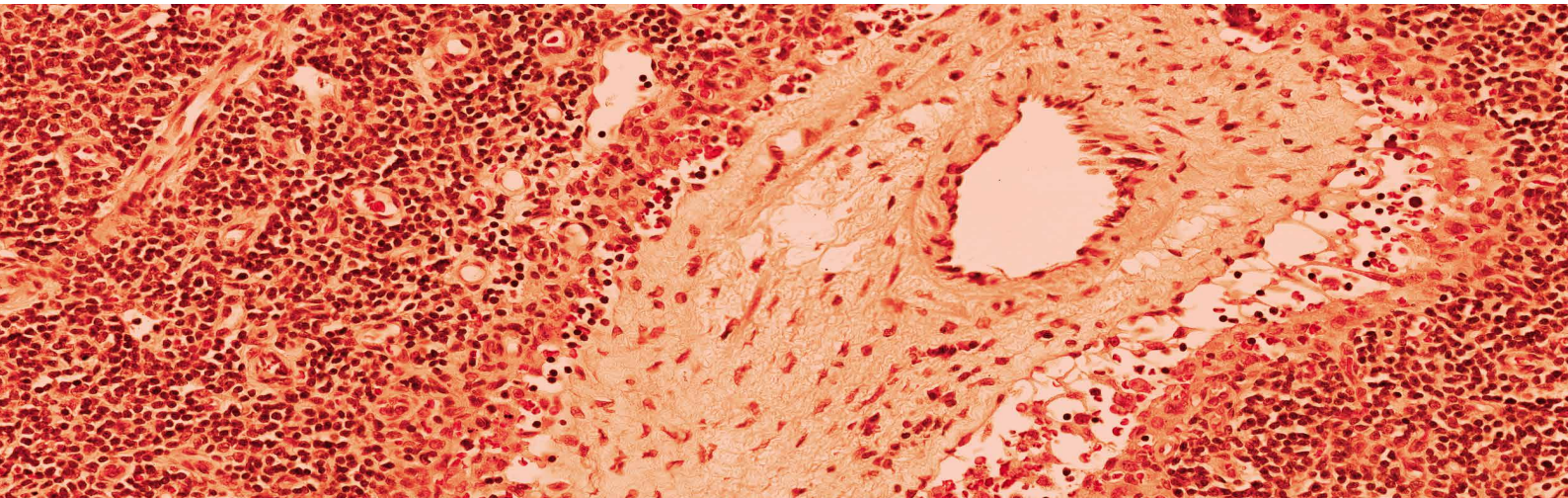
Intratumor heterogeneity and high plasticity account for therapy resistance. Causes of plasticity cell state transitions during tumor progression remain poorly understood. Here, we study genetically engineered mouse sympatho-adrenal tumors at several stages, from embryonic, pre-neoplastic hyperplasia to pheochromocytoma, neuroblastoma, and composite tumors. We deleted *KIF1B*β and *NF1* tumor suppressors in the embryonic mouse sympatho-adrenal lineage and observed pheochromocytoma, paraganglioma, neuroblastoma, and composite tumors arising in aged mice. Deep single-cell RNA sequencing combined with immunohistochemistry and RNA scope revealed chromaffin-neuroblast cell state transitions at embryonic and postnatal stages driving tumour plasticity. Cancer cells progressively adopt neuroblast lineage identity, computationally predicted to be mediated through a common chromaffin- neuroblast transitional, high-plasticity cell state.

Targeting Cyclin-dependent kinases for cancer therapy

Małgorzata Krajewska

University College Cork, Ireland

Cyclin-dependent kinases, with their role in transcription, cell cycle, and DNA damage repair, have been long recognized aspotential therapeutic targets in cancer. Transcriptional cyclin-dependent kinases (tCDKs) execute their function through phosphorylation of the C-terminal domain of RNA Pol II and other proteins involved in diverse cellular pathways. Using a combination oftranscriptomic and proteomic analysis, we uncovered a new function of tCDKs in mRNA processing of DNA damage response genes and identified new protein substrates likely involved in that regulation. The efficacy of tCDK inhibition in combination with otherinhibitors was tested in clinically relevant cancer models highlighting the therapeuticpotential of targeting tCDKs.



Targeting SF3B1 mutant cancers

Rachael Natrajan

Institute of Cancer Research, UK

Hotspot mutations in the RNA splicing gene SF3B1 are commonly found in cancer, where they lead to the global disruption of canonical splicing and are associated with a poor prognosis in several tumour types. SF3B1 mutations drive distinct signatures of alternative splicing through cryptic 3' splice site selection leading to global transcriptomic and proteomic changes. The functional consequences of the mis-splicing events in SF3B1 mutant cancers are poorly understood and approaches that exploit these events are not clinically available. Here I will discuss the strategies we are using in the lab to dissect the therapeutic vulnerabilities of SF3B1 mutant cells.

PARIS: A machine learning approach to find Synthetic Lethal Interactions in DNA Repair for Personalised Cancer Therapy

Özdemirhan Serçin

BioMed X, Germany

Synthetic Lethality is a powerful concept based on the genetic interaction events where the loss of function in two or more genes contributes together to loss of cell viability. Since its conception, it has been used for finding genetic interactions and pathways for cellular survival. Recently, this concept is also used to identify the "Achilles' Heels" of diseases, such as cancer. CRISPR/Cas9 knockout screens utilized by Broad Institute DepMap project aimed to create a genetic-dependency map of cancer cell lines. To analyze the DepMap knockout screen results using machine learning algorithms, we developed PARIS (PAn-canceR Inferred Synthetic lethalities). PARIS combines gene expression and mutation data with knockout screen results from DepMap project and generates a visual dependency map. In addition to known synthetic lethal partners, PARIS identified several novel synthetic lethal interactions. We studied two of them in detail: CDKN2A – TYMS and BRIP1 – ALDH2. CDKN2A is one of the most deleted tumor suppressors in cancers. We found that depletion of thymidine nucleotide pools by either knockout of TYMS or inhibition of Tyms by Pemetrexed caused cell cycle arrest and cell death. Similarly, in cells expressing low levels of Aldh2, aldehyde dehydrogenase, knockout of DNA helicase BRIP1 caused increased DNA damage and cell death. In conclusion, our analysis of DepMap knockout screen results using PARIS allowed us to identify new synthetic lethal interactions and they can be used for better stratification of patients for chemotherapy.

Photoimmunotherapy – from bench to bedside

Gabriela Kramer-Marek

Institute of Cancer Research, UK

Intraoperative near-infrared photoimmunotherapy (NIR-PIT) is a molecularly-targeted fluorescence-based theranostic approach which could become part of the armoury to improve the extent of cytoreduction by providing more optimal delineation of resection margins. Furthermore, the photochemical processes triggered by light irradiation of the conjugate may lead to specific and localised tumour cell killing, activating anti-tumour immunological responses stimulated by the release of tumour-associated antigens from ablated tumour cells.

Prof. Kramer-Marek will discuss how this regimen could significantly alter the therapeutic approaches against glioblastoma an extremely aggressive type of brain tumour.

Mapping the Immune Landscape of High-Risk Chemotherapy Resistant Breast Cancers

Sheeba Irshad

King's College London, UK

Purpose: To identify potential immunological targets in post-neoadjuvant chemotherapy (NAC) resistant Triple Negative Breast Cancer (TNBC) and ER+HER2- breast cancer (BC) disease.
Experimental Design: Following pathology review, one hundred and fifty-three patients were identified as having residual cancer burden (RCB)-II/III disease (TNBC n=80; ER+HER2- n=73). Baseline pre-NAC samples were available for evaluation for 32/80 TNBC and 36/73 and ER+HER2- cases. Bright field H&E assessment allowed for tumour infiltrating lymphocyte (TILs) evaluation in all cases. Multiplexed immunofluorescence was used to identify the abundance and distribution of immune cell subsets. Levels of checkpoints including PD1/PD-L1 expression were also quantified. Findings were then validated using expression profiling of cancer and immune-related genes. Cytometry by time-of-flight characterised the dynamic changes in the circulating immune cells with NAC.
Results: Residual cancer burden (RCB)-II/III TNBC and ER+HER2- BC were immunologically "cold" at baseline and end of NAC. Whilst the distribution of immune cell subsets across subtypes was similar, the mRNA expression profiles were both subtype- and chemotherapy-specific. TNBC RCB II/III disease was enriched with genes related to neutrophil degranulation; and displayed strong interplay across immune and cancer pathways. We observed similarities in the dynamic changes in B cell biology following NAC irrespective of subtype, however, NAC induced changes in the local and circulating TIME that varied by subtype and response. Specifically, in TNBC residual disease, we observed downregulation of stimulatory (CD40/OX40L) and inhibitory (PD-L1/PD-1) receptor expression and an increase in NK cell populations (especially CD56dimCD16-) within both the local TIME and peripheral white cell populations.
Conclusions: This study identifies several potential immunological pathways in residual disease, which may be targeted to benefit high risk patients.

IMMUNE SURVEILLANCE OF CELL PATHOLOGY IN CANCER and COVID-19: from the clinic to the bench and back to the clinic

Adrian Hayday

King's College London, UK
Francis Crick Institut , UK

αβ T cells and B cells can target cancer primarily via the capacity of their diverse antigen receptors to identify specific neo-epitopes resulting from genomic instability and mutation. γδ T cells also bear highly diverse antigen receptors, but they seemingly deploy them in a different way, focussed on the consequences of infection and cell transformation rather than on neo-antigens specific to pathogenic processes and/or infectious agents. This poses the challenge of how γδ T cells can distinguish dysregulated self from healthy self, thereby preventing inappropriate inflammation. This presentation will review our evidence for so-called "normality-sensing" wherein PDL1-like molecules expressed by healthy epithelial cells are detected by γδ TCR-dependent mechanisms, thereby suppressing the T cells' activation but maintaining their competence to respond to stress-antigens associated with cell pathology, as are typical of cancer and of virus infection. Evidence will be drawn from animal models of body surface immune surveillance; from studies of human breast and lung cancer; and from studies of COVID-19 patients, in all of which systems, γδ T cells display prominent potentially host-protective behaviours. We shall also consider the current application of this information in ongoing clinical trials of γδ T cell immuntherapeutics.

Oncogenic mechanisms of DIS3 mutations

Andrzej Dziembowski

International Institute of Molecular and Cell Biology, Poland

DIS3 encodes an essential catalytic subunit of the nuclear exosome complex. It is frequently mutated in multiple myeloma (MM). The role of mutated DIS3 alleles in oncogenesis remains unknown. In my talk, I will summarize our efforts to elucidate how DIS3 mutation drives oncogenesis.

Chemically Modified mRNA for Therapeutic Applications

Jacek Jemielity

University of Warsaw, Poland

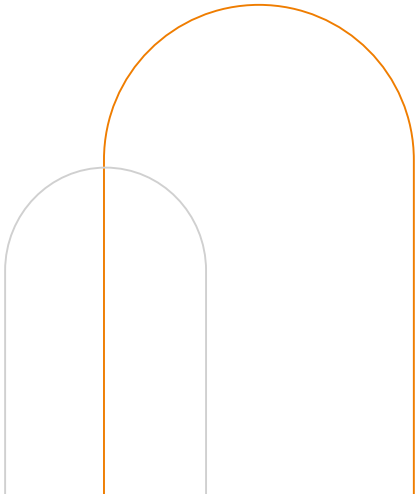
For several decades, scientists from all over the world have been trying to discover effective methods of combating diseases that are difficult to treat with traditional methods, such as cancer, genetic rare diseases, and the last two year in every aspect of our lives has been dominated by the pandemic caused by the coronavirus SARS-CoV-2. The hope for improving this situation is the so-called gene therapy, in which a therapeutic is delivered in the form of a genetic recipe, which is then expressed in the cells of the patient. In recent years, messenger RNA (mRNA), which is the genetic recipe for a specific protein, has received a great deal of attention in this context. A kind of culmination of these efforts was the development of mRNA vaccines against coronavirus, which were the first to be approved for widespread use. On the way to effective mRNA-based therapies, there have been a number of problems that have been solved, but there is also room for improvement. During the lecture, the speaker will present the idea of gene therapies and their enormous potential beyond anticancer and antiviral therapies. He will talk about the main problems associated with the development of this novel therapy and ways to solve them using biological and chemical methods, including those developed at the University of Warsaw.

Engineering messenger RNA nanotherapeutics for cancer therapy

Piotr Kowalski

University College Cork, Ireland

With the advent of messenger RNA therapeutics nanotechnology becomes increasingly important in pharmaceutical development. mRNA delivered with nanoparticles has been recognized as a safe andeffective therapeutic modality for protein expression, contributing to the success of SARS-CoV2 mRNA vaccines, and this technology has the potential to also revolutionize cancer therapeutics. Current strategies utilising mRNA nanotherapeutics for the treatmentof cancer focus on immunotherapy, including immunomodulators (e.g. cytokines), therapeutic vaccines, and antibodies. Our work has demonstrated the use of lipid nanoparticles for the expression of therapeutic antibodies against breast cancer.



P53 prevents genomic instability preserving epigenetic integrity

Ivano Amelio

University of Konstanz, Germany

Genetics is at the basis of cancer initiation and evolution, but substantial evidence indicates a role for epigenetics contributions to each individual stage of tumorigenesis. Failure of the cells to cope with epigenetic perturbations, caused by intrinsic factors or exposure to stressors, can produce irreversible damage, including genomic instability and cancer.

We report that the tumor suppressor p53 prevents genomic instability by preserving epigenetic integrity in stressed cells. p53-deficient cells display inability to cope and adapt to epigenetic perturbation; this condition impinges on global transcriptional regulation, DNA replication and mitosis ultimately leading to genomic instability. A status of metabolic stress underlies the vulnerability of p53-deficient cells; reversion of the metabolic status confers to p53-- cells the ability to prevent severe damage, resembling the response of p53 proficient cells.

Overall these data shed light on the molecular basis of p53-mediated regulation of genomic integrity and open to potential epigenetic vulnerabilities of therapeutic interests.

Found in Translation: Enabling Personalized Immunotherapy through Academic/Clinical alliances

Stephen Schoenberger

La Jolla Insitute for Immunology, USA

Translational research has the potential to move basic laboratory science to new therapeutic options for patients when alignment exists between the people and institutions involved in discovery and medicine. My talk will address our experiences in San Diego in which a novel approach to the identification of patient-specific tumor neoantigens (NeoAg) developed at the La Jolla Institute for Immunology, led to a set of phase 1 & 2 clinical trials at the UCSD Moores Cancer Center. The presentation will discuss both the scientific development of the NeoAg identification and personalized vaccine platforms and associated clinical data, but also the necessity of shared intention and resource allocation between the various stakeholders which is needed to avoid the pitfalls that too often preclude a successful connection between bench & bedside.

Dissecting immune microenvironment of gliomas at single-cell resolution allows for reprogramming of tumor microenvironment and improves immunotherapy

Bożena Kamińska – Kaczmarek

Nencki Institute, Poland

Glioblastomas (GBMs) are aggressive, lethal brain tumors that are massively infiltrated by myeloid cells supporting tumor growth and creating the immunosuppressive microenvironment (TME) blocking anti-tumor immunity and disabling immunotherapy. We employed Cellular Indexing of Transcriptomes and Epitopes by sequencing (CITE-seq) to reliably dissect myeloid components of TME, cell identities and states during progression of murine GL261 gliomas and spatial transcriptomics to localize cells of interest. Using computational approaches we identified fate trajectories and cell-to-cell interactions. We found the diversity of CD11b+ myeloid cells within the glioma TME: glioma-activated microglia are the major source of cytokines attracting other immune cells, whereas bone marrow-derived cells show the monocyte-to-macrophage transition and immunosuppressive phenotypes. This transition is coupled with a phenotypic switch from the IFN-related to antigen-presentation and tumor-supportive signatures. To target tumor supportive myeloid cells, we developed small synthetic peptides blocking specific glioma-myeloid cell interactions and new enzyme inhibitors which successfully altered functions of distinct immune cells in experimental gliomas. While those new inhibitors alone did not reduce tumor progression in vivo, they modified myeloid cells restoring their antitumor functionality improving immunotherapy outcome. As there are sex-dependent differences in the incidence rate, transcriptomic

profiles and GBM patient responses to a standard therapy, we studied myeloid cells using CITE-seq in gliomas in male and female mice. We found striking sex-dependent differences in transcriptional programs and composition of myeloid cells in murine gliomas. Higher abundance of protumor macrophages in males correlated with greater tumor size. Re-analysis of single-cell omics data from human GBMs revealed the predominance of inflammatory monocytes in female GBMs and abundance of protumor macrophages in male GBMs demonstrating higher expression of MCHII complex and PDL1. Our findings expand understanding of the complexity of anti-tumor immune responses in gliomas and may guide future therapies in consideration of patient sex.

Studies supported by a grant 2020/39/B/NZ4/02683 (National Science Centre Poland).

Glyco-immuno-regulation of epithelial disease

Richard Beatson

University College London, UK

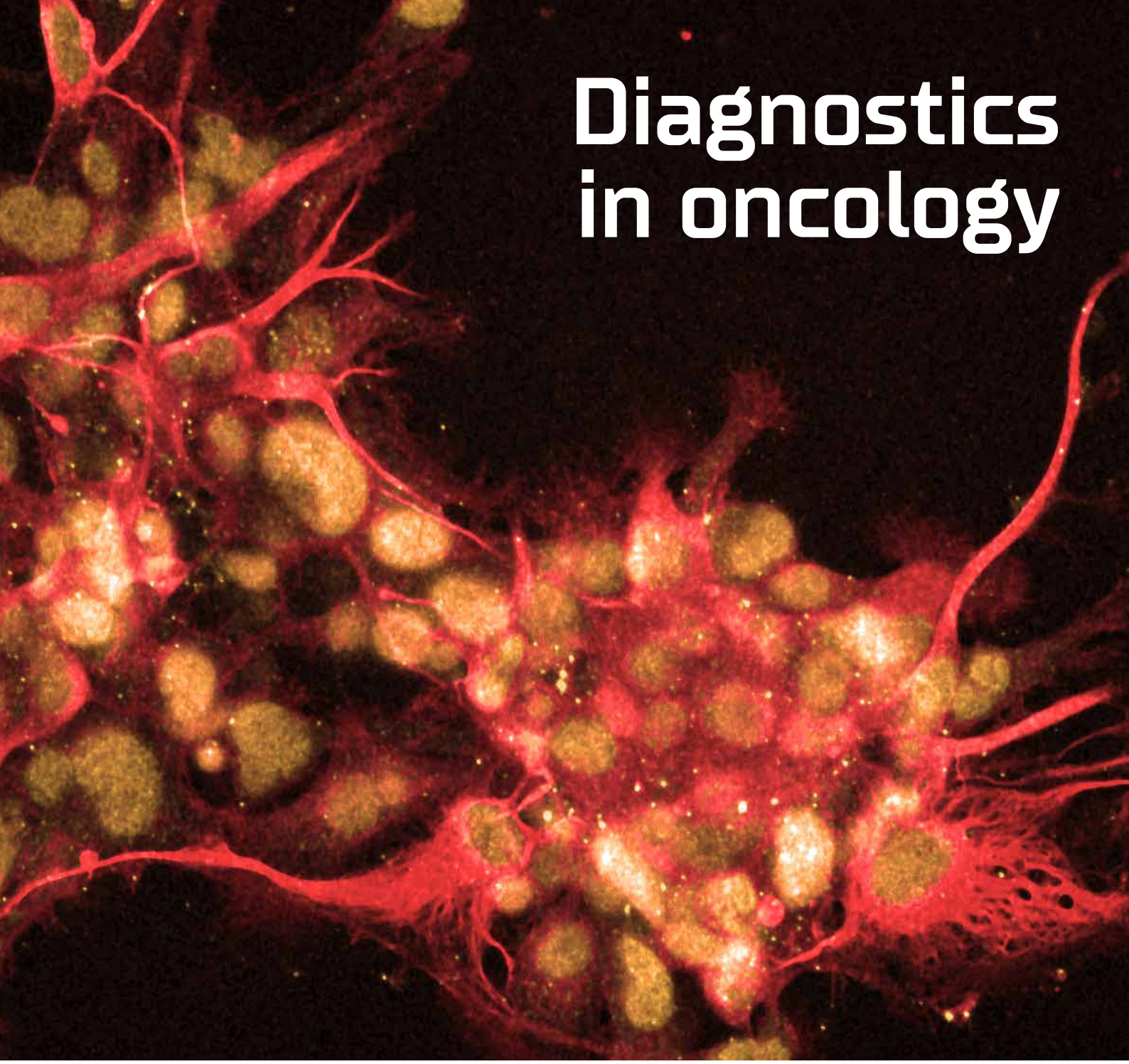
Hypersialylated glycans have been observed on the surface of diseased epithelial cells for over 60 years. Over the past decade, the glyco-immunology community has demonstrated that these sialic acids engage and educate the immune system to drive disease by binding to specific immunoreceptors called siglecs. An understanding of these processes is opening up large areas of therapeutic opportunity in diseases of chronically inflamed epithelium, including carcinomas.

Anti-cancer activity of ex vivo expanded γδ T cells against glioblastoma multiforme

Grzegorz Chodaczek

Łukasiewicz – PORT, Poland

Glioblastoma multiforme (GBM) is the most common malignant brain cancer with a median survival of approximately 10 months. Existing therapy, unfortunately, has very limited efficacy as cancer cells recur in 90% of cases. New therapeutic approaches of GBM treatment are desperately needed. One of the promising novel regimens may be immunotherapy – a type of cancer treatment that exploits the potential of immune system cells, in particular, cytotoxic T lymphocytes, to find and destroy tumor cells. Among the immune cell populations that demonstrate antitumor activity, innate-like T cells that carry T cell receptors (TCR) composed of γδ and δ chains (γδ T cells) are of particular interest. In humans, there are two major subsets of γδ T cells which were shown experimentally to exert anticancer functions in various settings: Vδ2+cells – dominant in the blood and Vδδ+ cells – mostly located in peripheral tissues. In our research, we compare effector functions of blood-derived and expanded Vδδ+ and Vδ2+ cells toward established GBM cell lines and primary GBM three-dimensional cell cultures to identify which subset is the most effective in cancer destruction. Our findings present differences in the killing of GBM cells between the subsets of γδ T cells and expand our knowledge about the potential of γδ T cells for their application in cellular immunotherapy.



Diagnostics in oncology

The tumor microenvironment in immunotherapy design and diagnostics – a personal journey

Tomasz Zal

Immatics, USA

Most favorable outcomes of immune therapies against cancer are noted for tumors that harbor large mutational load and dense immune infiltrates that are rich in T cells. In such situations, therapeutic immune responses can be unleashed by blocking immune checkpoints. This strategy has been remarkably successful in clinical practice for patients with immunologically "hot" tumor types, such as melanoma or lung cancer; yet, many patients with hot tumors and most with cold tumor types fail checkpoint therapies. To better understand the components of tumor microenvironment that recruit and modulate tumor infiltrating T cells, we have deployed multiple in vivo and ex vivo test systems in various tumor types and anatomical locations. In a common theme, our results highlight how intratumoral T cell behavior and therapy responsiveness depend on tissue stress and metabolic status.

Machine learning –based approaches capture novel prognostic morphological features in triple negative breast cancer patients

Anita Grigoriadis

King's College London, UK

Digital pathology provides new avenues to identify markers for diagnosis. I will present examples of machine learning based pipelines which have captured morphological patterns in tumours and lymph nodes, associated with molecular characteristics and indicative of disease progression in triple negative breast cancers.

How can morphological evaluation of the immune-system help in translational research?

Roberto Salgado

University Hospital of Antwerp, Belgium

There is a large body of literature on potential predictive biomarkers for immunotherapy ranging from TBM, LDH, Tumor Infiltrating Lymphocytes (TILs), PDL1, etc... Tumor Infiltrating Lymphocytes (TILs) are gaining importance as a biomarker in breast cancer. High TILs are associated with a better outcome and a better response to neoadjuvant therapy and immunotherapy in Triple negative and HER2 positive breast carcinomas, as well as having strong prognostic value in improving estimates of survival in early-stage TNBC treated with standard adjuvant/neoadjuvant chemotherapy (Level 1B evidence). This is based on an evaluation of TILs by pathologists at the time of diagnosis. Clinical utility using TILs as a biomarker for selection of patients for treatment with immune-checkpoint-inhibition is becoming important. PDL1-assessment in breast cancer is controversial with concerns on its reproducibility between pathologists and the fact that several PDL1-assays in Impassion130 predict outcome nearly as good as the approved companion diagnostic assay. TILs can be helpful to mitigate the current issues with PDL1-assays. The combined narrative of the importance of TILs in daily practice as a prognostic and predictive factor, together with PDL1, will be elaborated upon as this is becoming the most important predictive narrative for immunotherapeutic approaches in daily practice, and herewith may be very informative for translational breast cancer research.

New IT solution for guided reporting for pathologists diagnosing breast tumors

Krzysztof Żółtański

Vialutions, Poland

Andreas Pohling

Vialutions, Poland

Piotr Ziółkowski

Wroclaw Medical University, Poland
Hiscon, Poland

Breast cancer is one of the greatest challenges of modern oncology. On the one hand, in recent years the number of new diagnostic and therapeutic methods has significantly increased, thanks to which the response to treatment and survival rates have improved. On the other hand, still too many patients die from this disease.

The aim of our project was to develop, based on the existing medical standards and guidelines related to the accreditation of pathology facilities in Poland and other European countries, a user-friendly synoptic histopathology report of breast cancer samples.

In our opinion and the opinion of experts assessing the work on the report so far, it is a very useful and easy-to-use tool for pathologists involved in the breast cancer diagnosis.

Łukasiewicz – PORT

Timetable

WEDNESDAY 28.09.2022

15.00 – 15.15	Official opening (Michał Malewicz, Łukasiewicz – PORT)
SESSION 1	**BIOLOGICAL BASIS FOR CANCER (Rare diseases)**
15.15 – 15.50	Piotr Donizy (Wroclaw Medical University, Poland)
15.50 – 16.25	Agi Grigoriadis (King's College London, UK)
16.25 – 17.00	Lucy Yates (Wellcome Trust Sanger Institute, UK)
17.00 – 17.35	Sussane Schlisio (Karolinska Institute, Sweden)
17.35 – 18.00	Break
18.00 – 19.00	Opening Keynote: Bożena Kamińska – Kaczmarek (Nencki Institute, Poland)
19.00 – 19.30	Guided PORT Campus tour
19.30 – 21.00	Dinner at Łukasiewicz – PORT

THURSDAY 29.09.2022

SESSION 2	**BIOLOGICAL BASIS FOR CANCER (DDR)**
09.00 – 09.35	Małgorzata Krajewska (University College Cork, Ireland)
09.35 – 10.10	Rachael Natrajan (Institute of Cancer Research, UK)
10.10 – 10.45	Özdemirhan Serçin (BioMed X, Germany)
10.45 – 11.20	Break
SESSION 3	**PRECISION THERAPIES IN ONCOLOGY (Immuno-oncology I)**
11.20 – 11.55	Gabriela Kramer-Marek (Institute of Cancer Research, UK)
11.55 – 12.30	Sheeba Irshad (King's College London, UK)
12.30 – 13.05	Adrian Hayday (King's College London, UK; Francis Crick Institut , UK)
13.05 – 14.15	Lunch break
SESSION 4	**PRECISION THERAPIES IN ONCOLOGY (WIB – partners session)**
14.15 – 14.50	WIB presentation – Andrzej Dziembowski (IIMCB, Poland)
14.50 – 15.25	WIB presentation – Jacek Jemielity (UoW, Poland)
15.25 – 16.00	Piotr Kowalski (University College Cork, Ireland)
16.00 – 16.35	Ivano Amelio (University of Konstanz, Germany)
16.35 – 17.00	Break
17.00 – 18.00	Keynote lecture: Stephen Schoenberger (La Jolla Insitute for Immunology, USA)
19.30 – 21.00	Networking event: walk through Old Town followed by dinner on the river

FRIDAY 30.09.2022

SESSION 5	**PRECISION THERAPIES IN ONCOLOGY (Immuno-oncology II)**
09.30 – 10.05	Richard Beatson (University College London, UK)
10.05 – 10.40	Grzegorz Chodaczek (Łukasiewicz – PORT, Poland)
10.40 – 11.00	Break
SESSION 6	**DIAGNOSTICS IN ONCOLOGY (Biomarkers, new diagnostic methods/computational AI pathology)**
11.00 – 11.35	Tomasz Zal (Immatics, USA)
11.35 – 12.10	Anita Grigoriadis (King's College London, UK)
12.10 -12.45	Roberto Salgado (University Hospital of Antwerp, Belgium)
12.45 – 13.20	Piotr Ziółkowski (Wroclaw Medical University, Poland; Hiscon, Poland) Krzysztof Żółtański (Vialutions, Poland) Andreas Pohling (Vialutions, Poland)
13.20 – 15.00	Official closure, lunch

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Project selected for funding by the Ministry of Education and Science under the "Excellent Science" program, module "Support for scientific conferences". Grant application no.: DNK/SP/547342/2022

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