Poster Session Details

Session PO.MCB03.02 - RTK-ERBB-PI3K and New Targets in Therapeutic Resistance

3321 / 28 - Validating upstream kinase predictions by linking activity to drug target proximity

April 20, 2026, 2:00 PM - 5:00 PM Section 24

Presenter/Authors

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Abstract

Introduction: Sustained cell signaling is one of the hallmarks of tumor growth. Deregulation of kinase signaling can be studied by methods such as peptide microarrays or phospho-proteomics. For this, the prediction of kinases from phosphorylation signatures is a critical and complex. The aim of our study is to validate the biological relevance of kinase predictions, which we evaluate by the integration of kinase activity profiles with sensitivity data from the Genomics of Drug Sensitivity in Cancer (GDSC). A fundamental sensitivity mechanism involves repressing the activity of the drug's target kinase and its downstream survival pathways. We can test this mechanism through network analysis, hypothesizing that the signaling networks of active kinases and drug targets show high connectivity in sensitive cells, that should reflect the biological relevance of the kinase predictions.
Methods: Serine/Threonine Kinase (STK) activity profiling of 11 B-cell lymphoma cell lines was performed via the KinomePro platform (PamGene International B.V.). Kinases were predicted for 10 cell lines generally sensitive to multiple drugs (IC_{50} < 1 µm) compared to one relatively resistant control line (showing sensitivity to a smaller number of drugs). Cell line specific networks were generated from the top kinases and the target kinases of drugs the cells were most sensitive to, using the STRING protein-protein interaction database and Prize-Collecting Steiner Forest algorithm.
Results: To quantify signaling proximity of kinases and drug targets, we developed the network connectivity score. For each cell line, we calculated network connectivity using the median of the shortest paths between each kinase and drug target. This was then tested for statistical significance against a reference set of 50 random networks, generated using the original drug targets and randomized kinase data. Kinase predictions for 5 out of 10 B-cell lymphoma cell lines resulted in significant network connectivity score ($p < 0.07$), depending on the parameters used in the

prediction algorithm. These results demonstrate the method's utility to identify optimal parameter settings for the prediction algorithm.
Conclusion: We developed a validation method for the biological relevance of kinase predictions from phosphorylation signatures obtained in a cellular context. Future work will focus on applying this method to improve studies of the role of kinases in signal transduction by evaluating and optimizing the performance of kinase prediction methods and their potential biases.

Session PO.ET09.05 - Multi-Axis Antineoplastic Agents

5766 / 24 - Network-level kinase activity associate with differential drug sensitivity in B-Cell lymphoma cell lines

April 21, 2026, 2:00 PM - 5:00 PM Section 14

Presenter/Authors

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Abstract

Background: B-cell lymphomas display heterogeneous responses to kinase inhibitors, reflecting underlying variability in kinase activity and signaling network states. Understanding how baseline kinase activity and broader signaling network patterns relate to drug sensitivity could improve therapeutic stratification and uncover mechanisms of drug response.
Methods: Drug sensitivity data (IC_{50} values) for B-cell lymphoma cell lines were retrieved from the CancerRxGene database (Genomics of Drug Sensitivity in Cancer) and response variability for small-molecule inhibitors targeting serine/threonine kinase (STK) families was quantified using the standard deviation of its LN(IC_{50}) values across cell lines. For 11 B-cell lymphoma cell lines, kinase activity profiling was performed using KinomePro platform (PamGene International B.V.) and Upstream Kinase Analysis was used to predict kinases from the phosphorylation signatures. We conducted Multi-Omics Factor Analysis (MOFA) to integrate phosphorylation signatures and drug sensitivity data, identifying latent factors that capture correlations between kinases and drug responses.
Results: Drug responses showed substantial heterogeneity across cell lines: 7% of drugs were homogeneous (LN(IC_{50}) SD < 0.5), 41% moderately heterogeneous (SD 0.5-1), and 52% heterogeneous (SD > 1). In cell lines where drug sensitivity was observed, only 10-30% showed elevated activity of the drug target kinase, and this

correlation was not statistically significant. Correlation analysis (MOFA) identified latent factors that mapped kinase activity to drug sensitivity and revealed two distinct sensitivity clusters: one comprising PI3K/AKT/mTOR, central to cell growth, survival, metabolism, and proliferation; and a second cluster including CDK, ATM/ATR, Wee1, AURKA, and MAPK, central to DNA damage response, cell cycle regulation and checkpoint signaling. Upstream Kinase Analysis validated that cell lines sensitive to AKT/PI3K/mTOR inhibitors exhibited relatively high AKT and RSK signaling activity, whereas cell lines sensitive to inhibitors targeting cell cycle pathway showed higher baseline CDK and MAPK family kinases.
Conclusions: Our integrative analysis of drug sensitivity and kinase-activity data demonstrates that B-cell lymphoma response is shaped not only by individual kinase activities but also by the architecture of signaling networks. The strong concordance between baseline kinase activity signatures and drug sensitivity highlights network-level determinants of response. Signal-network signatures associated with sensitivity may serve as biomarkers for stratification and provide mechanistic insight into heterogeneous drug responses. These findings lay a foundation for functional validation and the development of combination therapies guided by network-level dependencies.

Session PO.ET02.05 - Antibody Technologies and Platforms 1

1663 / 22 - Monoclonal antibodies targeting the B-cell receptor complex directly induce widespread kinase inhibition and B-cell killing for the treatment of leukemia and lymphoma

April 20, 2026, 9:00 AM - 12:00 PM Section 11

Presenter/Authors

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Abstract

Welt Bio-Molecular Pharmaceutical (WBMP) aims to develop cytotoxic monoclonal antibody (mAb) therapies binding driver membrane receptors on malignant cells. Such membrane targets control growth, survival, and proliferation signals in healthy cells and their increased activity is often implicated in the oncogenesis of tumor cells. In B-cells, the B-cell Receptor Complex (BCRC), a signalosome comprising several membrane proteins, is involved in transmitting signals that determine cellular fate. Dysregulation of BCRC proteins, or those in downstream signaling pathways, result

in a diversity of B-cell cancer subtypes, making the BCRC a rational drug target. WBMP has previously described WBMP-4, a pro-apoptotic anti-membrane IgM antibody. Using a proprietary mAb-target-discovery platform, we have developed mAbs against two additional sites across the BCRC. All pipeline mAbs mediate apoptosis individually upon target binding. Here we investigate the therapeutic potential of this suite of mAbs via *in vitro* kinase and cytotoxicity analyses. Antibodies against designated regions of the BCRC, identified via WBMP's drug-discovery platform, were developed using hybridoma technology. Candidate mAbs were selected for their target-reactivity, and biologic effect was measured via preliminary growth assays of various lymphoma cell lines treated with hybridoma supernatant. These mAb supernatants have been tested for their ability to modulate B-cell kinase activity using the Pamgene phosphotyrosine kinome assay. Biacore assays will select unique, high affinity mAbs binding at distinct BCRC epitopes. Cell growth, MTT, and additional kinome assays will define the cytotoxicity characteristics of mAbs at varying doses and compared to existing B-cell therapeutics (i.e. ibrutinib, acalabrutinib, venetoclax, rituximab).
WBMP has successfully applied a drug discovery system to develop a pipeline of B-cell cancer therapeutics. Each candidate mAb in this pipeline binds to a specific BCRC epitope and modulates the function of this signalosome. Here we show the potent effect of each of these mAbs as monotherapies, *in vitro*, in inducing widespread kinase inhibition, and, at sufficient doses, apoptosis. Activity of these mAbs will be studied in mouse xenograft systems and safety will be assessed with comprehensive normal tissue and non-target protein cross-reactivity assays. Those mAbs which are determined to be safe and effective will be considered for further clinical development. Together, this pipeline of novel mAbs covers the spectrum of B-cell malignancies, and the availability of multiple, distinct, directly effective mAbs against B-cells offers the potential for combination treatment strategies that can be optimized for specific tumor-types.

Session PO.ET09.03 - Proximity-Induced Drug Discovery 1

4605 / 15 - Brigatinib based degraders as a therapeutic strategy for triple negative breast cancer

April 21, 2026, 9:00 AM - 12:00 PM Section 18

Presenter/Authors

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Abstract

Background: Treatment of patients with triple-negative breast cancer (TNBC) has been challenging due to the absence of well-defined molecular targets and high invasive and proliferative capabilities of these cells. Therefore, new therapeutic strategies for treatment of TNBC are urgently needed. Protease-targeted chimeras (PROTACs) are a class of emerging therapeutic inhibitors that recruit the ubiquitin E3 ligase to selectively degrade proteins. PROTAC degrader technology has shown robust results in inhibiting TNBC progression.

Methods: RNA sequencing and analysis were done. Samples were submitted to PamGene for kinome profiling and analysis. Western blotting was performed to visualize protein expression. MTT assays were carried out to evaluate cell viability. Colony formation assays assessed changes in clonogenicity. Data were analyzed using Graph Pad Prism Software 8 using one-way ANOVA and the unpaired two-tailed Students t-test. All data were evaluated in triplicate against control cells.

Results: Analysis of RNA sequencing in LM2-4175 TNBC cells treated with our target degrader showed increased genes associated with apoptosis and a decrease in genes associated with cell cycle checkpoint, DNA replication, and regulation of P53 signal transduction pathways. Kinase activity profiling of MDAMB231-LM2-4175 TNBC cells treated with our degrader showed a significant reduction in serine/threonine kinases (STKs) associated with Mitogen-activated protein kinase (MAPK) and cyclin-dependent kinase (CDK) families. In addition, we noticed a significant decrease in protein tyrosine kinases (PTK) associated with ephrin receptor proteins. Western blot analysis confirmed targeted degradation of Focal Adhesion Kinase in multiple TNBC cell lines (MDAMB-231-LM2-4175, MDAMB-468, and 4QXTB). MTT analysis of cell proliferation showed our degrader selectively targeted MDAMB231, MDAMB231-LM2-4175, MDAMB-468, and 4QXTB (Primary)TNBC cells over our non-neoplastic cell line, MCF10A, in a nanomolar range. Colony formation assays also showed our degrader was able to reduce clonogenicity in TNBC cell lines MDAMB231-LM2-4175, MDAMB-468, and 4QXTB.

Conclusions:Breast cancer is a diverse and intricate disease which is known to have unique inter- and intra-tumoral characteristics. We have identified a candidate PROTAC which can selectively target TNBC cells while minimally affecting normal bystander cells at nanomolar ranges in vitro. The further development of this degrader can serve as the fundamental basis for a novel therapeutic treatment in TNBC.

Session PO.TB05.02 - Pediatric Cancer Models

6179 / 15 - Differential sensitivity of paired FUS-TFCP2+ RMS PDX models developed from tumor specimens obtained prior to and after ALK inhibitor therapy

April 21, 2026, 2:00 PM - 5:00 PM Section 30

Presenter/Authors

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Abstract

FUS-TFCP2-positive rhabdomyosarcoma (FUS-TFCP2+ RMS) is a rare subtype of spindle cell/sclerosing RMS with a craniofacial predilection. These tumors are highly aggressive, quick to metastasize and evade conventional chemotherapies. FUS-TFCP2 fusion results in a gain of function transcription factor that promotes proliferation and activates survival pathways while blocking myogenic differentiation and inhibiting DNA repair. Currently, there is no effective standard of care, surgery can be difficult due to location and patients typically succumb to the disease within 15 months of diagnosis. Overexpression of downstream target, Anaplastic Lymphoma Kinase (ALK), is characteristic of FUS-TFCP2+ RMS. However, while case reports of targeted treatment with ALK inhibitors (ALKi) have shown modest results, resistance always emerges. In collaboration with the Pediatric Cancer Precision Genomics Program at the Riley Hospital for Children, we developed a paired set of FUS-TFCP2+ RMS patient-derived xenografts (PDXs). ALKi-sensitive PDX174 was derived from a patient tumor sample obtained prior to an 11-month ALKi (lorlatinib) regimen. Subsequently, a second sample was acquired following disease progression from which ALKi-resistant PDX199 was established. RT-PCR validated the fusion site in both models. In vivo studies confirmed PDX174 sensitivity and PDX199 resistance to lorlatinib (0.1mg/kg and 1mg/kg). Concordant with FUS-TFCP2+ characterization, transcriptome analysis showed significantly increased expression of ALK in both PDX174 (14.9-fold) and PDX199 (11.1-fold). Western blot analysis revealed robust overexpression of ALK isoforms in PDX174, whereas ALK expression in the ALKi-resistant PDX199 was only barely detectable. Instead, PDX199 exhibited

increased levels of TERT, CDK4/6, and BET proteins. To further compare the models, we utilized two complementary approaches to evaluate the activated kinome of ALKi-resistant PDX199 compared to ALKi-sensitive PDX174. Kinase activity profiling using PamGene peptide microarrays revealed a statistically significant increase in kinase activity of components involved in PI3K/AKT pathway and cell cycle CDKs (CDK1,2,4), with concomitant suppression of kinase activity of JNK/p38 MAPKs, indicating a shift toward PI3K/mTOR-driven pro-survival signaling and potential vulnerability to PI3K/AKT and CDK inhibition. Global kinome analysis using multiplexed inhibitor beads also showed an increase in CDK4/6 activation in ALKi-resistant PDX199 versus ALKi-sensitive PDX174. Pre-clinical models such as these provide a platform to connect molecular signatures with targeted therapy, increase our mechanistic understanding of tumor adaptive responses and design therapies that will mitigate the emergence of therapeutic resistance.

Session LBPO.ET03 - Late-Breaking Research: Experimental and Molecular Therapeutics 3

LB367 / 24 - Novel non saccharide glycosaminoglycan mimetic inhibit colorectal cancer stem cells by selectively targeting key tyrosine kinase receptors.

April 21, 2026, 2:00 PM - 5:00 PM Section 53

Presenter/Authors

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Abstract

Abstract is embargoed at this time.

Session PO.ET09.10 - Tyrosine Kinase, Phosphatase, and Other Inhibitors

5878 / 16 - Tumor Treating Fields remain effective in therapy-resistant glioblastoma with kinome shifts revealing novel therapeutic opportunities

April 21, 2026, 2:00 PM - 5:00 PM Section 18

Presenter/Authors

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Abstract

Glioblastoma (GBM) is the most common primary brain tumor in adults with a median survival of less than 15 months with maximal safe surgical resection, radiation, and the chemotherapy temozolomide. Addition of Tumor Treating Fields (TTFields), or alternating electromagnet fields therapy, to temozolomide was shown to extend the survival of GBM patients by approximately 4.9 months. TTFields disrupt mitosis to inhibit cell growth, but we also determined that TTFields alter the cellular kinome. Using a PamStation, we identified kinases that are predicted to be activated and repressed by TTFields treatment in newly diagnosed and recurrent GBM models that are sensitive or resistant to temozolomide or irradiation, respectively. While the growth of all GBM cells tested was significantly decreased by TTFields, there was a relatively limited set of kinases that were commonly altered in newly diagnosed and temozolomide-resistant GBM cells with little similarly across irradiation resistant GBMs. These kinase data are reminiscent of published data demonstrating kinome variability in radioresistant GBM xenografts. We did find that TTFields were predicted to activate PDGFRα in both newly diagnosed and temozolomide-resistant GBM cells: when combined with TTFields, a blood brain barrier penetrant PDGFR inhibitor, crenolanib, significantly decreased GBM cell growth. Subsequent studies have identified additional kinases to be evaluated in combination with TTFields in radioresistant GBM cells. Using the Novocure inovivo system, we plan to test these novel kinase inhibitor combinations with TTFields in mouse models bearing intracranial GBMs. We hope to identify a kinase inhibitor based treatment strategy that can be translated to the clinic to further improve TTFields mediated increases in patient survival.