breast cancer (BC), yet about 30% remain unresponsive. Since the potency of ICIs depends on the efficient presentation of tumor-specific antigens by cancer cells, compounds which increase such presentation could increase efficacy of ICIs. METHODS/STUDY POPULATION: A library of the ester and urethane derivatives of polyether ionophore antibiotic, monensin (MON) has been synthesized. MTT cell viability assays were performed on the panel of human and mouse BC cell lines, and non-cancerous breast epithelial cells to determine IC50 values of MON and its derivatives. Selectivity Indexes were calculated to identify the most selective compounds towards cancer versus non-cancer cells. Major Histocompatibility Complex (MHC) class I and II presentation and Programmed death-ligand 1 (PD-L1) expression have been determined using flow cytometry. Proteins involved in apoptosis, autophagy and immunogenic cell death were identified through immunoblotting. At least three biological replicates have been performed for each experiment. RESULTS/ANTICIPATED RESULTS: MON and several of its derivatives shown activity in nanomolar range against MDA-MB-231 human BC cell line. MON and its most potent derivatives significantly increased MHC class I and II presentation and downregulated the expression of PD-L1 in BC cell lines. DISCUSSION/SIGNIFICANCE: Present findings will lead to the development of new therapeutic approaches that can serve as single agents or be used in combination with existing ICIs for the treatment of metastatic BC. By pushing the boundaries of our understanding and developing new therapies, this research can make an impact in improving outcomes for patients with metastatic BC.

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The Analysis of N-glycans and Collagen to Predict Prostate Adenocarcinoma Outcome*

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OBJECTIVES/GOALS: Distinguishing indolent from aggressive prostate cancer and early identification of men at risk of developing aggressive, metastatic disease is of great importance. We aim to explore the relationship between N-glycan and collagen composition in prostate tumor tissue and the long-term outcome of the disease. METHODS/STUDY POPULATION: Matrix assisted laser desorption/ionization mass spectrometry can be utilized to characterize N-glycan profiles in formalin fixed paraffin embedded tissues. Collagen may also be characterized using ECM-targeted collagenase MALDI imaging. These approaches were used to analyze prostatectomy samples with different clinical outcomes. Tissue microarrays containing tissues from 75 non-progressors (no evidence of disease; NED) and 50 metastatic cases (MET) were examined. From a combined list of 90 N-glycans and 500 collagenase peptides, the average AUC intensity value for each glycan and collagen peptide was extracted and assessed as a predictor of metastatic progression. Ancestral informative markers were analyzed and polygenic hazard risk scores were generated for samples as well. RESULTS/ANTICIPATED RESULTS: Three N-glycans and three collagen peptides were found to discriminate between NED and MET cases with statistical significance. The best performing N-glycan was Hex6HexNAc6Fuc1 with an AUC of 0.77 ($p<0.001$). While the best performing collagen peptide was COL1A2 with an AUC of C 0.77 ($p<0.001$). DISCUSSION/SIGNIFICANCE: Both a collagen peptide and N-glycan were discovered as promising biomarkers to predict metastasis. Future validation studies are needed to confirm biomarker potential and to determine if the addition of these biomarkers can strengthen current genomic classifier's ability to predict metastatic prostate cancer.

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Pathogenicity of a CCDC6-RET Fusion in Malignant Peripheral Nerve Sheath Tumor (MPNST)

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OBJECTIVES/GOALS: RETgene fusions in sarcoma are rare and their impact on pathogenicity is unknown. Malignant peripheral nerve sheath tumors (MPNST) are a deadly, genomically heterogenous soft tissue sarcoma rarely harboring targetable aberrations. We present a case of a CCDC6-RET fusion MPNST sensitive to RET-inhibitor therapy in a xenograft model. METHODS/STUDY POPULATION: Lung tumor tissue was obtained per an approved collection protocol from a 21yo male patient with a spontaneous MPNST harboring an inactivating mutation in NF-1 and a CCDC6-RET gene fusion detected by a commercially available sequencing panel (Signatera). To confirm pathogenicity of the RET fusion, fresh tumor tissue was engrafted into immunocompromised NSG mice in the anterior and posterior flanks, harvested at ~10 weeks, and re-transplanted into bilateral flanks. When tumor diameters reached 0.5-1cm (~4 weeks), mice were randomized into 3 groups (n=6/group) and treated with either vehicle (V) (PBS), the RET-specific inhibitor selpercatinib (S) (20mg/kg twice daily), or the multi-kinase inhibitor cabozantinib (C) (30mg/kg daily) by oral gavage. Mice were monitored weekly for weight and tumor size. RESULTS/ANTICIPATED RESULTS: 92% (33/36) of implanted tumors were evaluable for treatment response. Pre-treatment tumor volumes (mm3) across all three groups were similar (mean/Std Dev – V: 230/111, S: 271/132, C: 230/123). At day 7, tumor growth was significantly inhibited by S and C versus V (ANOVA $p < 0.001$, post-hoc Tukey's V vs S $p= 0.0178$, V vs C $p< 0.0001$, S vs C $p= 0.0005$). V-treated tumors increased in volume by 60% while S reduced tumor volume by ~80% and C reduced tumor volume by ~20%. S and C treatments were tolerated well. and S improved survival with 100% of mice alive at day 63 vs 0% in V and C groups. 6 of the 12 implanted tumors treated with S, 50% increased in size after ~6-weeks following a >90% initial tumor reduction in tumor volume. Follow-on molecular studies in S-resistant tumors are ongoing. DISCUSSION/SIGNIFICANCE: Targetable genomic changes in MPNST, especially in RET, are infrequent and often considered stochastic. Our findings suggest that precision medicine approaches pairing genomic sequencing and in vivotesting of target gene pathogenicity may guide treatment planning and novel discovery for rare, difficult to treat sarcomas.

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Prototyping a mobile phone application for Chimeric Antigen Receptor (CAR) T-cell therapy patient monitoring and data collection post-discharge

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OBJECTIVES/GOALS: Research objectives include prototyping a mobile phone application that allows physicians to monitor CD19-directed CAR T-cell therapy patients remotely after discharge. This app will also enable standardized data collection across different

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