Oral Presentation – 01

TAp73β regulates the Wnt/β-catenin signaling pathway in a zebrafish xenograft model in Hepatocellular Carcinoma

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Introduction and Aim: Hepatocellular carcinoma (HCC) is the most common type of liver cancer. Preclinical studies are essential in the identification of new targets for HCC treatments. However, most of the data obtained from in vitro studies and in vitro models have several limitations in predicting cancer's biology. Recently, zebrafish xenograft model has become popular because of its cost-effectiveness, in vivo dynamic visualization of tumor growth. This study aimed to investigate the interaction between TAp73β and Wnt/β-catenin signaling pathway in a HCC zebrafish xenograft model.

Materials and Methods: First, we tested the effect of TAp73β expression on β-catenin activation in HCC cell lines by western blot, immunofluorescence and luciferase studies. Then we examined the β-catenin expression and localization under the TAp73β expression in a zebrafish xenograft model. Finally, we performed a β-catenin rescue assay by ectopic expression of Axin-1, and we examined the effect of TAp73β-induced Wnt/β-catenin signaling pathway activation on the metastatic abilities of HCC cells using the zebrafish xenograft model.

Results: Our results showed that TAp73β significantly increased the expression of phospho-b-catenin (Ser675) and its nuclear localization in HCC cells. We also showed that TAp73β activated the Wnt/β-catenin pathway in HCC cells. In addition, overexpression of TAp73β overexpression increased the nuclear localization of active p-β-catenin (Ser675) in the zebrafish xenograft model. Moreover, overexpression of Axin-1 caused the degradation of β-catenin and inhibited TAp73β-induced metastasis

Conclusion: Consequently, our results indicate that TAp73β increases HCC cell metastasis through β-catenin activation in a zebrafish xenograft model.

Keywords: Hepatocellular carcinoma, p73, metastasis, Wnt/β-catenin pathway, zebrafish xenograft

Oral Presentation – 02

Naive and TLR4 Stimulated Adipose Derived Mesenchymal Stem Cells Inhibit EMT and Metastasis of Pancreatic Ductal Adenocarcinoma Cells

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Introduction: In order to intervene in the dense desmoplastic tumor microenvironment, it is important to first elucidate the interactions between cells. To investigate the potential antitumorigenic effects of adipose-derived MSC(ADMSC) on the pancreatic ductal epithelial cell Panc-1, we aimed to investigate the effects of both proinflammatory and anti-inflammatory ADMSC phenotypes on EMT and metastasis.

Material and method: ADMSCs were treated with TLR4 agonist and antagonist. Pro-inflammatory and anti-inflammatory characters were determined according to their responses to cytokines. An indirect co-culture model was established using 0.4 µm inserts and Panc-1 and ADMSCs were cultured at a ratio of 1:10. Next, gene expression levels of CDH1, VIM, ZEB1 and CLDN1 were evaluated for EMT analysis. Analysis of vimentin and E cadherin proteins was also evaluated by immunofluorescence staining. Metastatic potential was also analyzed by gene expressions of MMP2, KDR, PLAU, MMP9, TIMP1, IGF2R and COL1A1.

Results: At the end of the 96h, naive and proinflammatory ADMSCs increased the expression of CDH1 and CLDN1 of Panc-1 cells and decreased the expression of VIM gene. In metastasis related genes, it significantly decreased the expression of MMP2, KDR, MMP9, TIMP1, IGF2R and COL1A1 genes, except for the PLAU gene. ADMSCs with anti-inflammatory character, showed opposite effects.

Conclusion: Both naive ADMSCs and proinflammatory ADMSCs were showed antitumor effects on Panc-1 cells. Anti-inflammatory ADMSCs were showed tumor promoting effects. Understanding the role of MSCs in the tumor microenvironment will be a guiding factor for the development of microenvironment-targeted therapeutic approaches in the future.

Keywords: Pancreatic cancer, Mesenchymal stem cell, TLR4, Tumor microenvironment.

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Oral Presentation – 03

Investigating The Effects of Temozolomide on The Viability of Glioblastoma Stem Cells Responsible for Recurrence Using a 3D Culture Model

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Introduction and Aim: Glioblastoma (GB) is the most lethal brain tumor. The inevitable recurrence after initial treatment has been the most challenging for GB. The presence of GB stem cells (GSCs), which cause the recurrent GB untreatable and the main cause of recurrent, is currently lacking effective therapeutic options. In this regard, we aim to evaluate the behaviors of GSCs in a more realistic approach by utilizing a 3D scaffold for the brain environment and develop a more effective treatment by targeting GSCs.

Materials and Methods: We developed a 3D scaffold using bacterial cellulose that incorporates hyaluronic acid and collagen for 3D culture studies. The structure of the scaffold was demonstrated through FTIR and SEM analysis. The attachment of GSCs to the scaffold was demonstrated using Ki67, Nestin, and DAPI staining techniques. GSCs were seeded using a suitable medium cocktail for 2D and 3D scaffold cultures. The main aim of this experimental design was to compare the Temozolomide (TMZ) dosage in 2D and 3D cultures; thus, cell viability was determined using Live&Dead analysis.

Results: The data demonstrate that when 2D and 3D GSC cultures are treated with TMZ, the dosage required for 3D cell culture is four times higher than that for 2D cell culture. This result significantly indicates the impact of the cell environment on their viability.

Conclusion: Creating 3D environments that closely mimic reality can bridge the gap between clinical and in vitro experiments, improving treatment efficacy.

Keywords: glioblastoma stem cells, 3D culture, Drug exposure, Tumor microenvironment

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Oral Presentation – 04

Drug Repositioning to Specifically Target Multıple Myeloma Subtypes Based in silico Investigation of Differentıal Gene Expression Profiling

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Introduction and Aim: Multiple myeloma (MM) is a malignancy that develops in a kind of white blood cell known as a plasma cell. The aim of this study is to propose a new treatment for MM and its genetically distinct subtypes which clinical treatment success rate is still low. This project used bioinformatics analysis to reposition existing licensed drugs in accordance with differential gene expression profiles discovered from patient-specific datasets by using NCBI-GEO in order to find potential pharmacological roles for MM.

Materials and Methods: Gene Expression Omnibus 2R (GEO2R) was used to analyze top differential genes in patients. Subsequently, for each comparison, a STRING database was created and transferred to Cytoscape for representing protein-protein interactions. Drugs capable of inhibiting hub genes identified for each comparison were recorded using DrugBank and PubChem. Finally, in silico toxicity analysis was performed to determine whether the drug is appropriate for usage by using SwissADME.

Results: The most up-regulated genes were determined for MM and its subtypes. The protein-protein interaction maps of the most up-regulated 150 genes were created and reduced to 10 hub genes. A total of 227 candidate drugs were identified for targeting these hub genes. Drugs that target the selected gene, but are FDA approved under MM or any cancer types are not included in the study. According to the mentioned parameters and toxicity analyses, the candidates were reduced to 16 drugs.

Conclusion: Finally, the candidate drugs currently in use with non-cancer purposes are promised for each MM subtype.

Keywords: DEG, drug repositioning, multiple myeloma, toxicity

Oral Presentation – 05

Exploring New Frontiers in HGSOC Treatment: Targeting Drug Resistance with miRNA Mimics

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Introduction and Aim: High-grade serous ovarian cancer (HGSOC) is the predominant histological subtype of epithelial ovarian cancer. Despite the success of first-line chemotherapy, and approval of PARP inhibitors, significant portion of patients develop resistance leading to poor outcomes. Therefore, identifying regulators of drug resistance and new treatment strategies is essential.

MicroRNAs (miRNAs) have been shown to play significant roles in cancer progression by acting as either tumour suppressors or oncogenes. However, the specific targets of miRNAs in ovarian cancer remain largely unknown. Therefore, this study aimed to explore the role of miRNAs in drug response, and resistance in HGSOC.

Materials and Methods: 40 FFPE samples of patients with HGSOC were used, and miRNA expression was analysed using microarray and qRT-PCR assays. Resistant HGSOC cells were generated through a stepwise dose-escalation method. miRNA-mimics were transfected into the resistant cells, and their interactions with conventional therapies were examined.

Results: The study found that let7b-5p and 188-5p were significantly downregulated in both the resistant FFPE samples and *in vitro* resistance models. Based on the results of combinational drug and miRNA-mimic treatment, upregulation of miR188-5p using miRNA mimic resensitize Olaparib resistance cells and increase apoptotic cell death.

Conclusion: This study sheds light on the role of miRNAs in drug resistance, and progression in HGSOC. The findings of this study may contribute to the development of alternative treatment options for HGSOC, improving patient outcomes.

Keywords: HGSOC, miRNA, drug-resistance

Oral Presentation – 06

Flavopiridol Inhibits Cell Proliferation and Migration in Pancreatic Ductal Adenocarcinoma Cells

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Introduction and Aim: Flavopiridol, a semi-synthetic flavonoid analog of an alkaloid called Rohitukine, was shown to have anti-inflammatory and antioxidant effects. Although it is known to be a pan-CDK inhibitor, its detail cellular mechanisms related to the anti-tumorigenic potential are still unclear. Here, we aimed to investigate the therapeutic potential of flavopiridol in pancreatic ductal adenocarcinoma (PDAC) cells through cell proliferation and migration.

Materials and Methods: MiaPaca-2 and Panc-1, as human PDAC cell lines, and HPDE, as a non-tumorigenic human pancreatic ductal epithelial cell line, were used in cell proliferation and migration analysis. MTS assay were performed in MiaPaCa-2, Panc-1, and HPDE cells treated with 5, 10, 25, 50, 100, 200, 400, 500, 600, 800, 1000 nM doses of flavopiridol for 24h, 48h and 72h. To confirm the cyclin inhibition and investigate the anti-metastatic potential, Cyclin D1 mRNA expression and migration were analyzed by RT-PCR and wound healing assay, respectively, in Panc-1 cells.

Results: Based on our MTS results, flavopiridol significantly inhibits the PDAC cell proliferation, but not HPDE cells, especially in 100 nM and 200 nM doses for 48h. Flavopiridol mediated Cyclin D1 inhibition was almost completely proven by RT-PCR in Panc-1 cells with 100 nM and 200 nM doses for 48h. Additionally, flavopiriol decreased the cell migration in Panc-1 cells with enhanced dose and time dependent manner.

Conclusion: Flavopiridol is a powerful anti-tumorigenic, anti-metastatic and anti-proliferative agent for PDAC cells. However, its specific detail mechanisms of action need to be investigated in pancreatic cancer.

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Oral Presentation – 07

Sphingosine 1-Phosphate Signaling in Midostaurin Resistance in FLT3-ITD Positive Acute Myeloid Leukemia

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Introduction and Aim: ITD mutation in the FLT3 gene, found in 20-25% of AML cases, leads to continuous activation of FLT3, promoting cell proliferation and inhibiting apoptosis. Midostaurin, an FDA-approved drug targeting FLT3-ITD, is used for AML treatment. Resistance to treatment poses a challenge in the clinic. This study aims to explore a novel approach by targeting SK-1, an anti-apoptotic sphingolipid with roles in multi-drug resistance, in combination with midostaurin.

Materials and Methods: Basal levels of SK-1 was evaluated in midostaurin resistant and sensitive FLT3-ITD+ AML cells. The antiproliferative effects of SK-1 inhibition combined with midostaurin on resistant and sensitive cells were investigated. Combination indexes were analyzed to determine whether SK-1 inhibition enhances the efficacy of midostaurin to overcome resistance. The apoptotic effects of the combinations were evaluated through caspase-3 and PARP activation.

Results: The resistant cells exhibited elevated levels of SK-1 compared to the sensitive cells. Compared to midostaurin treatment, midostaurin and SK-1 inhibitor combination significantly decreased cell viability in midostaurin resistant cell lines. Synergistic effects of the combination treatment were observed in both midostaurin resistant and sensitive cells. Apoptosis induced via cleaved PARP and cleaved caspase-3 levels in combination group compared to control and midostaurin treated group.

Conclusion: Our findings show that SK-1 plays an important role in drug resistant in FLT3-ITD+ AML cells. Targeting SK-1 successfully increases the efficacy of midostaurin in midostaurin resistant cells and induces apoptosis in both resistant and sensitive cells making it a potential therapeutic target to overcome acquired midostaurin resistance.

Keywords: FLT3-ITD, FLT3 inhibitor, sphingosine kinase 1, drug resistance, apoptosis

Oral Presentation – 08

Evaluation of CSRP1 Expression as a Prognostic Marker in Colorectal Cancer

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Introduction and Aim: Colon cancer is a leading cause of cancer-related death worldwide. Despite developments in the clinical management of this disease, currently, around 60% of patients with colon cancer are expected to survive 5-years. In this study we aimed to evaluate cysteine-rich protein 1 (CSRP1) which encodes a member of the cysteine-rich protein family as a prognostic marker in colorectal cancer.

Materials and Methods: Publicly available bulk and single-cell transcriptomic data (scRNA-seq) of colon tumors were downloaded from GEO database and GDC data portal. Raw data processing was performed using RMA and DESeq2 methods for microarray and bulk RNA sequencing data, respectively. scRNA-seq data was processed via Seurat R package.

Results: Bioinformatic analyses showed that high expression of CSRP1 was associated with poor overall and recurrence-free survival. Multivariate analysis revealed that CSRP1 expression was a significant poor prognostic predictor independent of MSI status, TNM stage and KRAS-BRAF mutation status. CSRP1 expression had significant positive correlation with the expression of mesenchymal markers ($p<0.001$). When the consensus molecular subtypes of colon cancer (CMS) was considered (1), CMS4 type tumors had the highest CSRP1 expression. Analysis of a scRNAseq dataset (GSE178318) of colon tumors revealed that CSRP1 was expressed mainly by epithelial cells and CAFs (unpublished data).

Conclusion: CSRP1 expression was associated with a mesenchymal and aggressive molecular profile in colorectal cancer. The prognostic value of this putative biomarker needs to be validated in independent cohorts.

Keywords: Colorectal Cancer (CRC), CSRP1, prognosis, transcriptomics, bioinformatics

Oral Presentation – 09

Dual Targeting of Glycolysis and Glutaminolysis as a Strategy to Inhibit Tumor Cell Proliferation

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Introduction & Aim: Activating mutations of the oncogenic-KRAS is common in several types of tumors, including pancreatic ductal adenocarcinoma (PDAC). Increased glycolysis and glutaminolysis are two prevalent metabolic phenotypes that can be controlled by activated KRAS signaling. Given that a recent study showed that KRAS induction sensitizes pancreatic ductal epithelial cells to dual inhibition of 6-phosphofructo-2-kinase/fructose-2,6-bisphosphatase-3 (PFKFB3) and glutaminase (GLS1), key enzymes of glycolysis and glutaminolysis, respectively, we aimed to examine whether co-targeting of PFKFB3 and GLS1 exhibits an antiproliferative effect on tumor cells lines of various origin with or without mutant KRAS.

Material & Methods: PFKFB3 and GLS1 activities were inhibited pharmacologically using AZ-PFKFB3-26 and CB-839, respectively. Cell proliferation was determined by crystal violet staining. Western blot was used to analyze PFKFB3 and GLS1 proteins. Fructose-2,6-bisphosphate (F2,6BP) levels were analyzed using an enzyme-coupled assay.

Results: Simultaneous inhibition of GLS1 and PFKFB3 exhibited a much greater anti-proliferative effect on HCT116 and Mia PaCa-2, both of which harbor KRAS mutations, and H1299, which has a wild-type KRAS, than either inhibitor alone. While short-term (8 hours) GLS1 inhibition did not affect PFKFB3 protein levels, PFKFB3 inhibition decreased GLS1 protein levels, suggesting a functional interaction between PFKFB3 and GLS1. Further, although GLS1 inhibition did not affect PFKFB3 protein levels, it reduced F2,6BP levels, suggesting that GLS1 activity may be required for a fully active PFKFB3.

Conclusion: Co-inhibition of PFKFB3 and GLS1 may prove effective in preventing tumor cell proliferation, regardless of KRAS mutation status.

Keywords: Pancreatic adenocarcinoma, KRAS, PFKFB3, GLS1

Oral Presentation – 10

Effect of PKR Kinase Activation on the sensitivity of choriocarcinoma cells to chemotherapy agent

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Introduction and Aim: Choriocarcinoma is a gestational disease that originates from trophoblasts, is a malignant tumor with proliferation of abnormal placental trophoblast cells. We aim to determine how proliferation, apoptotic properties will change as a result of PKR activation. we investigated whether PKR activation can be an alternative combination strategy in cancer treatment, by determining the sensitivity of choriocarcinoma cells to the chemotherapeutic agent doxorubicin during PKR activation.

Materials and Methods: In choriocarcinoma cells, poly I:C LPS were treated to activate PKR, cell viability was determined using a cell counter to determine the effect of doxorubicin. Viability, apoptosis pathways, necrosis were examined by looking at the effect of doxorubicin in cells in which we created PKR activation by poly I:C/ LPS treated swan 71 cells by performing flow cytometry experiment. Western blot analysis was applied to determine the protein-level expression of p-PKR in Swan 71 cells.

Results: Doxorubicin was found to dose-dependently inhibit cell viability from swan 71 cells. It was found that sensitivity to doxorubicin in swan 71 cells treated with Poly I:C /LPS showed resistance to PKR activation compared to controls. Upon further investigation we determined that doxorubicin killed cells by apoptosis. PKR activated cells were moderately less sensitive to doxorubicin compared to controls. Interestingly, we observed that PKR phosphorylation greatly inhibited in the cells treated with doxorubicin upon Poly I:C, LPS treatment.

Conclusion: It has been observed that PKR activation increase resistance to the chemotherapy drug doxorubicin in choriocarcinoma cells.

Keywords: PKR activation, choriocarcinoma, apoptosis

Oral Presentation – 11

Investigation of the Effects of Chloroquine on Proteasomal System in Glioblastoma Stem Cells

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Introduction and Aim: Glioblastoma (GBM) is a highly lethal and aggressive malignant disease of the brain. The success rate of standard therapy is quite low because of the recurrence. The main reason for the recurrence of the neoplasm is the remaining glioblastoma stem cells (GSCs) in the resected area. It is predicted that a treatment plan based on the stem cells will increase the efficacy of GBM treatment. Chloroquine (CQ) is an autophagy inhibitor drug and many studies have shown that it has beneficial effects in various malignancies. Since one of the most important regulators of cell homeostasis is the closely linked proteasomal system and autophagy pathways, we aimed to investigate the effects of CQ on the proteasomal system of GSCs.

Materials and Methods: GSCs were cultured with appropriate medium cocktails. Cells were treated with CQ. Proteasomal activity assay and western blotting were performed to analyze the proteasome subunits expression levels.

Results: CQ treated GSCs expressed lower levels of proteasomal α4, α6, β1, β2, and β5 subunits. In addition, the cells showed some decrease in K48 polyubiquitination. In parallel with these findings, the cells showed a decrease in their proteasomal activity, as expected.

Conclusion: The proteasomal system and autophagy pathway enhance tumor cell survival under treatment conditions. The results show that CQ attenuates the activity of the proteasomal system within the cell. A potential GBM therapeutic approach involving CQ may hold promise for patients in the future.

Keywords: Glioblastoma, Glioblastoma Stem Cells, Chloroquine, Proteasome, Proteasomal Activity

Oral Presentation – 12

Indoximod Restricts Tumor Growth by Targeting Breast Cancer Viability

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Introduction and Aim: Breast cancer is the second most common cancer in women having potential to metastasize through the lymph and blood circulation.IDO(Indoleamine 2-3 dioxygenase) is an enzyme highly expressed in neoplastic cells and tumor leukocytes.Enhanced IDO activation in different cancer cells causes T cells to lose their proper function.Nowadays,IDO inhibition has received much attention in the field of cancer immunotherapy.Indoximod,an IDO inhibitor involved in the regulation of immune responses.In this study,we hypothesized that Indoximod restricts tumor growth by targeting cell viability in metastatic breast cancer.Herein,we aimed to interpret the possible effects of IDO inhibition on tumor cells and changes in immune responses.

Material and Methods: *In vitro* and *in vivo* experiments were designed using 4T1 metastatic breast cancer cell line.4T1 cells were supplemented with TNF-α for mimicking tumor microenvironment.Annexin V staining was performed to investigate apoptosis.For *in vivo* experiments, Control(n=5),4T1(n=10) and 4T1+Indoximod(n=10) groups were generated.$1x10^6$ cells were orthotopically injected into the mammary tissues of Balb/C female mice.One week later,Indoximod was administered intraperitoneally twice daily.Tumor sizes were measured twice a week.29 days after tumor injection, blood was collected from the eye socket of the animals. Peripheral blood smear analysis was performed to evaluate the immune responses. Moreover, primary and metastatic tissues were excised and analyzed.

Results: Indoximod significantly reduced 4T1 cell viability by inducing apoptosis. Tumor sizes were reduced after Indoximod injection in experimental model.We observed less metastatic regions in group 4T1+Indoximod compared to group 4T1.Moreover,enhanced immune responses in group 4T1 were detected,while immune responses were reduced in group 4T1+Indoximod.

Conclusion: Indoximod induces apoptosis thereby restricting tumor growth and metastasis.

Keywords: Breast cancer, 4T1, Indoximod, Apoptosis, Metastasis

Oral Presentation – 13

Apoptotic Effects of Paclitaxel/Aloe-Emodin Combination in MCF-7 and MDA-MB-231 Breast Cancer Cell Lines

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Introduction and Aim: Cancer is a group of diseases characterized by uncontrolled cell proliferation and has different clinical manifestations and treatments. Breast cancer is the second leading cause of cancer-related deaths worldwide, following lung cancer. Due to the high cost and concerning side effects of conventional cancer treatments, there has been a growing interest in natural and herbal alternatives. Many cancer treatment studies are focused on drug discovery from herbal compounds. In this study, we aimed to investigate the apoptotic effects of aloe-emodin and paclitaxel on estrogen receptor-positive (MCF-7) and estrogen receptor-negative (MDA-MB-231) human breast cancer cell lines.

Materials and Methods: We assessed the effects of combined treatment with aloe-emodin, a herbal anthraquinone derivative, and paclitaxel on cell death through apoptotic pathways in MCF-7 and MDA-MB-231 cells. This was accomplished by analyzing annexin V binding, total caspase activity, and cell cycle distribution.

Results: The combination treatment of paclitaxel and aloe-emodin significantly induced apoptosis in MCF-7 and MDA-MB-231 cell lines, leading to enhanced cell death and cell cycle arrest.

Conclusion: Combining plant-derived compounds with cytotoxic agents to achieve more effective results in cancer treatment is a widely explored approach. However, there is a lack of sufficient studies on the combined use of aloe-emodin and paclitaxel in the literature. Hence, our study holds significant importance in this context.

Keywords: Aloe-emodin, Apoptotic effect, Breast cancer, Paclitaxel

Oral Presentation – 14

miR-30b-3p regulates apoptosis in CD8+ T lymphocytes in triple negative breast tumor bearing mice

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Introduction and Aim: Breast cancer had been regarded as immune-cold cancer type until the last decade. Recent studies have revealed breast cancer exhibits different immunological states based on subtypes. Especially, triple negative breast cancer (TNBC) stands out immunologically. Despite the recognized role of miRNAs as key regulators in immune cells, studies on breast cancer remain limited. This study aimed to investigate miRNA profiles in CD8+ T cells during the formation and remission of TNBC in vivo model.

Materials and Methods: TNBC model was established with 4T1 cells and Balb/c mice. Spleen-derived CD8+ T cells were isolated from control, primary tumor and remission groups. miRNA profiling was performed with microarray. miRWalk3.0 target prediction and WebGestalt-KEGG pathway enrichment analysis tools were used. Validations of miRNAs and mRNAs were performed by qPCR. Detection of apoptosis was done by flow cytometry.

Results: Microarray analysis showed that mmu-miR-30b-3p emerged as the most significant differentially expressed common miRNA among the comparisons. qPCR analysis confirmed its upregulation in primary tumor group, while expression of miR-30b-3p was low in remission group. Bioinformatic analysis revealed miR-30b-3p regulates apoptosis, particularly by targeting anti-apoptotic genes BCL-2 and BCL-XL. Validation experiments showed that decreased expression of BCL-2 and BCL-XL in CD8+ T cells from primary tumor group resulted in increased apoptosis. Conversely, remission group showed elevated expression of target genes, suggesting suppression of apoptosis in CD8+ T cells.

Conclusion: mmu-miR-30b-3p may contribute to immune evasion of tumor cells in TNBC through apoptosis and could serve as an immunological biomarker for CD8+ T cell responses against tumor cells.

Keywords: Triple-negative breast cancer, Adaptive immune system, miRNA

Oral Presentation – 15

PTEN R234W Variant: A Novel Case Presentation in Non Small Cell Lung Cancer Patients

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Introduction and Aim: PTEN is a strong tumor suppressor gene, with mutations being found in around %5 of NSCLC cases. The aim of this study is to investigate mutations and prognosis of NSCLC harboring PTEN mutations.

Materials and Methods: A total of 24 patients with NCSLC who had not yet undergone chemotherapy were recruited for the study between 2021-2023. We conducted liquid biopsy analysis using the Onco/Reveal-cfDNA-Multicancer Panel by NGS. To predict variants deleterious effects, we used SIFT(v5.2.2) and PolyPhen-2(v2.2.2) in silico tools via Pivat software. I-Mutant2.0 software evaluated aminoacid substitution's impact on protein stabilization.

Results: In our study, the frequency of PTEN-R234W was observed in %16,7(4/24) of the cases, and histologically, it was detected in %25(4/16) of the cases diagnosed with SCC. It has been associated with hereditary diseases. In our study, no hereditary disease was identified in the epicrisis of stage 3A cases 8th and 17th carrying this variant. Additionally, the epicrisis of case 18th(stage-4A) and 22nd(stage-4B), both with this mutation, could not be accessed. According to the PolyPhen2 and SIFT analysis programs, the potential effect of this variant on protein function was determined to be probably damaging(0.971) and tolerated(0.12), respectively. Due to the I-Mutant analysis, it was observed that this SNP has a destabilizing effect on protein stabilization.

Conclusion: The R234W variant is the first SCC report associated with the oncogenesis process. This variant has been reported as a VUS in the Clinvar databases. Therefore, further studies are needed to determine its clinical significance.

Keywords: non-small cell lung cancer, in silico tools, clinical significance, liquid biopsy

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Oral Presentation – 16

Expressions of GSTO1, GSTP1, GSTM1, GSTS1 isoenzymes in NSCLC tissues

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Introduction and Aim: Glutathione S-Transferases (GSTs) are Phase II enzymes which are involved in metabolism of various xenobiotics including the drugs. GSTP1 and GSTM1 isoenzymes have the role of protecting the lung tissue by catalyzing the conjugation of carcinogens with glutathione. In this study, we investigated the immunohistochemical staining characteristics of GSTOmega (GSTO1), GSTpi (GSTP1), GSTmu (GSTM1), p38, bcl-2 and caspase-3 in adenocarcinoma (n=20) and squamous cell carcinoma (n=20) lung tumor tissues from 40 patients.

Materials and Methods: Non-small cell lung cancer (NSCLC) tissues of patients were compared according to their immunohistochemical staining intensity from the patients. Relationships between GSTO1, GSTP1, GSTM1, p38, bcl-2 and caspase-3 expressions in carcinoma tissue were examined by the Mann Whitney-U test, and the clinicopathological data were examined by the Spearman correlation rank test.

Results: The results showed that GSTO1, GSTP1, GSTM1, p38, bcl-2 and caspase-3 expressions were significantly higher in lung tumor group than benign lung group ($p<0.01$). However, *no statistically significant differences* in the level of GSTSigma1 protein expression between tumor and benign lung groups ($p>0.05$)**.** p38, caspase-3, bcl-2 and GSTSigma expressions were positively correlated in the tumor group ($p<0.01$). The higher expressions of GSTP1, GSTM1 and caspase-3, p38 **in tumor group** could be important in lung cancer progression and development.

Conclusions: As a result, the difference of the GSTO1, GSTP1, GSTM1 isoenzymes expressions between the groups show that they play an important role in the diagnosis of NSCL carcinoma.

Keywords: GST, Non-Small Lung Carcinoma, Apoptosis

Oral Presentation – 17

Generating single-barcode harbouring cell lines from chemotherapy resistant Caco-2 cell line to study drug resistance.

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Introduction and Aim: Resistance to cancer therapeutics can inevitably lead to treatment failure through the selection of drug resistant clones. Quantifying the drug resistance has begun to be possible with the advent of single-cell barcoding approach whereby frequencies of selected clones harbouring unique cellular barcodes can be determined. It was aimed to establish single barcode harbouring chemotherapy-resistant Caco-2 cells to characterize barcode frequencies.

Materials and Methods: Lentiviral barcode library was used to integrate cellular barcodes into initial Caco-2 cell line before the establishment of their chemotherapy-resistant derivatives. To identify the mechanism of resistance, whether pre-existing or de novo drug resistance was in place, amplicon-based NGS approach was carried out. Drug resistant barcoded Caco-2 cells was faced to single cell dilution assay to establish a new cell line from harbouring a single barcode. Barcode characterization and validation of single barcode in a newly generated drug resistant Caco-2 cell lines was validated.

Results: The results demonstrate a cellular barcoding technology incorporated with single-cell dilution approach to establish single-cell derived colonies under the chemotherapeutic selection pressure in Caco-2 cells. The barcoding approach show the frequencies of barcode enrichment under drug resistant derivatives of Caco-2 cells. Moreover, unique-barcode harbouring drug-resistant Caco-2 single cell-derived cell lines exhibited the suitability of this experimental model system to study drug resistance at the single-cell resolution.

Conclusion: The power of monitoring drug resistance at the single cell level with the advent of recently developed cellular barcoding technology provides capacity to exploit the tumour's vulnerability.

Keywords: drug resistance, barcoding

Oral Presentation – 18

The Effect of Boron Compounds on Androgen Signaling in Prostate Cancer

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Introduction and Aim: Progression of prostate cancer is largely dependent on androgen receptor (AR) and AR related signaling pathways. Second-generation non-steroidal anti-androgens (enzalutamide) used for androgen ablation therapy have some side effects and moreover they often lead to the formation of highly aggressive castration-resistant tumors. Therefore, it is extremely important to develop new therapeutic approaches that will prevent the formation of resistant tumors. Studies have reported that boron compounds are promising agents in the treatment of prostate cancer. In this context, our study aimed to investigate the efficiency of boric acid and patented boron compounds in the regulation of AR signaling pathway and target genes.

Material and Methods: For this purpose, the effect of boron compounds on AR and its target genes such as PSA, NKX3.1 and NFκB was investigated by MTT, immunoblot, immunoprecipitation and qRT-PCR.

Results: In our results, it was determined that patented boron compounds have a higher cytotoxic effect and more importantly they act as a chemosensitizer by increasing the efficacy of enzalutamide. Furthermore, it was found that M7m reduced the level and activation of AR and its target genes most effectively. However, we observed that M7m inhibits AR nuclear translocation and also increases its degradation. Eventually, it was observed that M7m leads to a decrease in mRNA levels of the target genes.

Conclusion: It was concluded that blocking the AR signaling pathway, which plays a critical role in the development of castration-resistant prostate cancer, via boron compounds may offer an important therapy option.

Keywords: Prostate Cancer, Boron Compounds, Enzalutamide, AR Signaling

Oral Presentation – 19

Investigation of CD40, CD40L Gene Variants and sCD40, sCD40L Serum Levels in Laryngeal Cancer

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Introduction and Aim: Genetic factors can influence how our immune system functions and potentially affect the development of cancer. Laryngeal cancer is a prevalent form of head and neck cancer. Our research aimed to explore the influence of alterations in the CD40 (rs1883832) and CD40L (rs1126535) genes, as well as the levels of their corresponding proteins in the bloodstream, on the progression of laryngeal cancer.

Materials and Methods: We performed PCR-RFLP to genotype SNPs in 96 patients diagnosed with laryngeal cancer and 127 healthy individuals. Additionally, we measured the circulating levels of sCD40 and sCD40L using ELISA.

Results: A significant difference was noticed in genotype between those with laryngeal cancer and healthy individuals for the CD40 gene (rs1883832). It has been found that the C allele is the dominant gene variant and individuals with the CC variant are at a greater risk of developing laryngeal cancer. The study found that although there was a difference in genotype between the patients and the control group, this did not correspond to a difference in sCD40 levels. The patient group was found to have a significant correlation between the levels of sCD40 and sCD40L, with a correlation coefficient of 0.52 and a p-value of less than 0.01.

Conclusion: Based on our findings, the CD40 (rs1883832) polymorphism we identified in patients with laryngeal cancer could serve as a marker for determining an individual's risk of developing this type of cancer.

Keywords: Laryngeal Cancer, CD40, CD40L, sCD40, sCD40L

Oral Presentation – 20

MicroRNA-145's Regulatory Role in Breast Cancer Progression

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Introduction and Aim: MicroRNAs (miRNAs) have emerged as focal points in cancer research, particularly tumor suppressor miRNAs like miR-145, which are suggested to play a vital role in cancer diagnosis and prognosis. This study aims to explore the potential of miR-145 expression in breast cancer as a biomarker for early diagnosis, prognosis prediction, and staging. The findings could underscore miR-145's clinical significance as a biomarker, potentially advancing novel approaches for early diagnosis and treatment of breast cancer.

Materials and Methods: This study analyzed miR-145 expression profiles using blood samples from 300 individuals, including 200 breast cancer patients and 100 healthy controls. RNA extraction followed a standardized method. The extracted RNA was reverse transcribed into complementary DNA (cDNA) using Reverse Transcriptase and miR-145 specific stem-loop miRNA primer. Finally, Real-Time qPCR was used to analyze miRNA-145 expression changes at cancer patient stages.

Results: Significant miR-145 expression differences were observed between groups. Statistical analyses revealed noteworthy distinctions in mean miR-145 expression levels between healthy controls, stage 1, stage 2, stage 3, and stage 4 patient groups ($p<0.001$ for each). The control group exhibited higher miR-145 expression compared to patient groups ($p<0.001$ for each). Fold change rates (fold change $2^{-\Delta\Delta CT}$) decreased in patient groups (stage 1, stage 2, stage 3, and stage 4) compared to the control group.

Conclusion: These findings support miR-145's tumor suppressor role as documented in the literature. Therefore, an association between breast cancer stage advancement and downregulated miR-145 expression can be inferred.

Keywords: miR-145, breast cancer, fold&change, tumor suppressor

Oral Presentation – 21

Investigation of methylation and expression levels of the guanine nucleotide-binding protein gamma-7 (GNG7) gene in oral squamous cell carcinoma

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Introduction and Aim: Oral squamous cell carcinoma (OSCC) is responsible for more than 91% of all malignancies in oral cavity. Epigenetic alterations and other environmental factors can cause changes in gene expression of OSCC pathogenesis. DNA methylation is just one of many epigenetic alterations. Herein, in our study we focused on predictive biomarker potential of guanine nucleotide-binding protein γ-7 **(***GNG7*) gene methylation. The clinical significance of *GNG7* methylation and the association with oral carcinogenesis is still remain unknown.

Materials and Methods: DNA and RNA samples of tissues and body fluids obtained from OSCC patients and healthy individuals were used to examine the methylation and expression levels of the *GNG7* gene by using QMSP/QRT-PCR methods, respectively. All results were compared with clinicopathological and demographical parameters.

Results: *GNG7* gene hypermethylation was observed in 18% of patients. It was observed decreased expression levels in 48% and increased expression levels in 32% OSCC patients. There was a statistical significance was found between the classification of retromolar trigone with tongue, floor of the mouth and decreased expression levels. Decreased expression levels of *GNG7* gene in tumor, matched-normal tissues were downregulated in patients than healthy individuals and *GNG7* gene expression levels in patients and healthy individuals' serum were seen abundant significance.

Conclusion: The *GNG7* gene promoter hypermethylation depends on loss of expression in OSCC patients. The result of loss of expression due to the existence of tumor hypermethylation compared to healthy people suggests that there is a specific subgroup of OSCC patients for the *GNG7* gene in Turkish population.

Keywords: Oral squamous cell carcinoma; *GNG7* gene; Epigenetics; Expression; Methylation

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Oral Presentation – 22

Increasing Treatment Efficacy by Drug Repositioning in Acute Lymphoblastic Leukemia

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Introduction and Aim: Acute lymphoblastic leukemia (ALL) is a malignant hematological cancer that is caused by different genetic alterations. The most common subtype of ALL is the Philadelphia positive ALL (Ph+ALL), which carries the BCR/ABL translocation, the most aggressive and high-risk subtype due to imatinib resistance among ALL subtypes. This research aims to analyze the cytotoxic activity and drug combination efficiency of three drugs Maytansine, Desipramine, Glipizide which are determined by meta-analysis of bioinformatics approach, on sensitive and Imatinib resistant Ph(+) and also Ph(-) ALL cell lines.

Materials and Methods: SUP-B15 and Jurkat cell lines were used as a Ph(+) and Ph(-) ALL cell lines respectively. Initially, SUP-B15 cell line was treated with Imatinib with increased concentration generate drug resistant cell line (SUP-B15/R). Additionally, Jurkat cells were treated with Maytansine. SUP-B15 and SUP-B15/R treated with desipramine and Glipizide to determine their cytotoxic effects on cell lines by MTT Assay. Finally, cytotoxic drugs were also applied in combination with Imatinib to detect possible synergistic effect.

Results: SUP-B15/R cells achieved 8-fold Imatinib resistance. IC50 and IC20 values of each agent were determined. Combination therapy of Imatinib with desipramine and Imatinib with Glipizide showed increased inhibitory effect on cell proliferation compared to the treatment by drugs alone.

Conclusion: The use of repositioned drugs, whose cytotoxic effects have been determined, in both Ph(-) ALL and Ph(+) ALL patients may pave the way to increase the survival rate by increasing the efficacy of the treatment, including overcoming imatinib resistance.

Keywords: ALL, drug resistance, imatinib, repurposing, philadelphia chromosome

Oral Presentation – 23

HDAC Inhibitor Induces Mitochondrial Membrane Potential Disruption and Reverses the Epithelial-Mesenchymal Transition in Colorectal Cancer

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Introduction and Aim: Colorectal cancer (CRC), which arises from genetic and epigenetic alterations, is a major contributor to cancer-related mortalities worldwide. Despite many chemotherapy options, the outcomes underline the need for a better understanding of the underlying tumorigenic mechanisms. Histone deacetylases (HDACs), known for their role in gene expression regulation and malignant behaviors, are targeted by HDAC inhibitors, whose anticancer mechanisms vary based on cancer type. This study examines the effects of combined Quisinostat and 5-Fluorouracil (5FU) therapy on CRC cell death and epithelial-mesenchymal transition.

Methods: HCT116 cells were treated with Quisinostat, 5FU, and a combination of both. Cell viability and apoptotic changes were assessed using resazurin reagent and a Mitochondrial Membrane Potential kit, respectively. Epithelial-Mesenchymal Transition changes were evaluated through immunofluorescence staining using E-cadherin and vimentin as markers.

Results: IC50 for 5FU was found to be 84 µM as per the viability analysis. For Quisinostat, an IC50 could not be determined, prompting the use of the highest concentration (20 nM) that did not show statistical significance, in the combined treatment. The combination treatment caused a significant rise in Mitochondrial Membrane Potential disruption and E-cadherin levels, compared to 5FU alone.

Conclusion: The results imply that Quisinostat-5-FU combination could potentially enhance drug sensitivity in CRC, thus offering a promising new treatment approach. Combinatorial therapy disrupts the Mitochondrial Membrane Potential, possibly leading to increased cancer cell death, and induces an increase in epithelial characteristics, hinting at a reversal of Epithelial-Mesenchymal Transition, which may limit cancer metastasis. These promising findings necessitate further exploration and validation.

Keywords: Colorectal cancer, Histone deacetylases, Drug sensitivity, Apoptosis, Epithelial-mesenchymal transition

Oral Presentation – 24

Evaluation of Sulfasalazine Drug Repurposing Potantial and Sulfasalazine Encapsulated PLGA Nanoparticles in Non-Small Cell Lung Cancer

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Introduction and Aim: Drug development for Non-Small Cell Lung Cancer (NSCLC) is challenging and new therapeutic options are needed due to high mortality rate. Drug repurposing could speed up the drug discovery process by reducing the pharmacokinetic uncertainty and offering a solution to the global burden of cancer as well as NSCLC. In addition, nanoparticles are used to enhance pharmacokinetic properties of drugs. The aim of this study is to evaluate the potential of repurposing sulfasalazine (SSZ) as a therapeutic agent for NSCLC, to synthesize PLGA encapsulated SSZ nanoparticles (SSZ-PLGA NPs) and to study its effect on A549 cell line via MTT assay.

Materials and Methods: SSZ-PLGA NPs were synthesized by using single emulsion solvent evaporation method and characterized by determining encapsulation efficiency, drug loading percentage, particle sizes, zeta potentials and release profiles. Cell viabilities were determined by applying the MTT assay on both A549 and HUVEC cell lines for both SSZ and SSZ-PLGA NPs. HUVEC cells are used as control cells.

Results: Size and zeta potentials of SSZ-PLGA NPs ranged between 220nm to 360nm and -17,7mV to -9,21mV, respectively. MTT analysis revealed the effectiveness of SSZ on A549 cell line. IC_{50} is determined as 1,197mM.

Conclusion: This study presents the **synthesized** SSZ-PLGA NPs which can be a promising candidate according to cell viability and *in vitro* release profile studies. Primary results revealed anticancer effect of SSZ on NSCLC. The effect of SSZ alone and SSZ-PLGA NPs will further be studied in molecular level.

Keywords: Drug repurposing, Sulfasalazine, NSCLC, PLGA nanoparticles

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Oral Presentation – 25

Biological Effects of CRISPR/Cas9-mediated Knockout of RAB27A in SCLC

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Introduction and Aim: Small cell lung cancer (SCLC) is characterized by rapid growth and early metastasis. Identifying new molecular targets are important in the pathogenesis of SCLC in order to develop new treatment strategies. RAB27A is the critical protein for intracellular exosome trafficking and is a driver of tumour progression. However, demonstrating the potential impact of suppressing RAB27A in SCLC as therapeutic approach is an important deficiency.

Materials and Methods: *RAB27A* gene knockout SCLC cell lines were generated using a CRISPR/cas9 system. qRT-PCR, Western blotting and Sanger sequencing were performed to confirm *RAB27A* knockout in SCLC cells. TEM and EXOCET assays were used to detect the alteration of exosomes. Proliferation and colony formation were detected by MTT and microscopy. Subsequently, we intrapulmonally injected N417 and H524 SCLC cells (control and RAB27A knockout for each cell) into SCID mice. The effects of RAB27A knockout on mouse tumor model were analysed using 18F-FDG PET/CT scans.

Results: Knocking out RAB27A significantly decreased the expression of CD9, CD63, Tsg101, exosome secretion and exosomal protein in SCLC*($p<0.0001$)*. We found that RAB27A knockout dramatically reduced proliferation and colony formation in SCLC cells *($p< 0.001$, $p<0.0001$).* Furthermore, *RAB27A* knockout decreased proliferation and especially metastasis in mouse model (*$p<0,0001$*).

Conclusion: These studies clearly demonstrated that RAB27A plays an important role in the pathogenesis of SCLC, and targeting the *RAB27A* gene in SCLC cell lines significantly reduces the activity of the exosomal pathway. *RAB27A*, therefore, can be a promising cancer therapeutic strategy.

Keywords: RAB27A, exosome, SCLC, CRISPR/Cas9, Carcinogenesis

Oral Presentation – 26

Determination of In Vitro and In Vivo Effects of Taxifolin and Epirubicin on Epithelial-Mesenchymal Transition in Mouse Breast Cancer Cells

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Introduction and Aim: The aim of our study was to investigate potential effects of Taxifolin (Tax) on enhancing the effectiveness of Epirubicin (EPI) in treating breast cancer (BC), specifically in 4T1 cells and an allograft BALB/c model.

Materials and Methods: To examine the effects of Tax and EPI, both individually and in combination, we performed cell viability assays (MTT) and cytotoxicity assays (LDH) in 4T1 cells. In addition, we implanted 4T1 cells into female BALB/c mice to conduct in vivo studies and evaluate the therapeutic efficacy of Tax and EPI alone or in combination. Tumor volumes and histological analysis were also assessed in mice. To further understand mechanisms involved, we examined mRNA and protein levels of EMT-related genes, as well as active Caspase-3/7 levels, using qRT-PCR, western blot, and enzyme-linked immunosorbent assays, respectively.

Results: In vitro results demonstrated that the co-administration of Tax and EPI reduced cell viability and cytotoxicity in 4T1 cell lines. In vivo, co-administration of Tax and EPI suppressed tumor growth in BALB/c mice with 4T1 BC. Additionally, this combination treatment significantly increased the levels of active Caspase-3/7 and downregulated mRNA and protein levels of N-cadherin, β-catenin, Vimentin, Snail, and Slug, but upregulated E-cadherin gene. It significantly decreased mRNA levels of Zeb1 and Zeb2 genes.

Conclusion: We concluded that the co-administration of Tax and EPI is efficient in inhibiting BC growth compared to EPI alone. Therefore, our results suggest that Tax has the potential to be a promising agent in clinical treatment of highly aggressive BC patients.

Keywords: Epirubicin, Taxifolin, Breast cancer, 4T1 cells, Epithelial mesenchymal transition

Oral Presentation – 27

Molecular and Bioinformatic Investigation of Proteomic Differences Between Cancerous and Normal Tissue Samples of Colorectal Cancer Patients*

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Introduction and Aim: New treatment strategies targeting the factors that play a critical role in the transition from normal cells to malignant cells are urgently needed. Therefore, we believe that the discovery of novel targets may generate new treatment options and cancer biomarkers. The aim of this study was to identify the proteins whose expression changes between colorectal cancer and normal tissues using the proteomics tools.

Materials and Methods: In order to determine the differentially expressed proteins between the tissue samples, the label-free nLC-MS/MS method was used for the proteomic analysis. The statistically significant proteins were then uploaded and analyzed using the Metascape portal to determine the affected biological process. The experimentally determined proteins were also compared with proteomic data generated by CPTAC via the UALCAN platform.

Results: A total of 77 proteins were identified as statistically significant using proteomic analyzes between cancerous and normal tissues. Using the Metascape web portal, the biological processes involved were determined. The expression profiles of the 77 proteins were compared with CPTAC data using the UALCAN portal. It was found that 45 of the 77 proteins clearly matched the CPTAC results.

Conclusions: The results of this proteomic study performed with clinical samples from patients are very valuable, and if the results are validated with different methods such as ELISA with serum samples from patients, it may lead to the discovery of new biomarkers for colorectal cancer diagnosis.

Keywords: Colorectal Cancer, Proteomics, Label-free nLC-MS/MS, Metascape, CPTAC

The study was funded by the Scientific and Technological Research Council of Türkiye (TÜBİTAK) with Project no 121S170.

Oral Presentation – 28

The Impacts of Ceramidase Inhibition with D-E-Mapp Sln Formulation upon Cell Death Mechanism in Breast Cancer as an in-vitro and in-vivo models.

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Introduction and Aim: Sphingolipids regulate various biological processes such as growth, proliferation, migration, invasion and metastasis by controlling signaling functions within the cancer cell signaling network. Breast cancer is the most common type of cancer among women. While advances in the early diagnosis and treatment of breast cancer in recent years have led to a significant reduction in mortality, these advances have been insufficient to completely cure the disease. The aim of this study was to investigate the cytotoxicity of D-e-MAPP, a ceramidase inhibitor, and D-e-MAPP SLN formulation on 4T1 cells *in vitro* and the changes in 4T1-induced breast tumor tissue in BALB/c mice *in vivo* by immunohistochemistry.

Materials and Methods: Cytotoxicity was tested by MTT test. For *in vivo* experiments mice were injected with 4T1 breast cancer cells to form breast tumors. They were then treated with D-e-MAPP and D-e-MAPP SLN formulations.

Results: The results showed that D-e-MAPP and its SLN form exerted cytotoxicity at low doses in 4T1 cells. *In vivo* results indicated that positive staining of ER, PR and CerB2 oncogene antigens were determined in control group of tissues. While, the p53 staining in the D-e-MAPP and D-e-MAPP SLN treated groups was positively arisen compared to control tissues as well as staining of ER, PR, and CerB2 was slightly decreased.

Conclusion: We believe that the results of the research on the application of D-e-MAPP and its SLN form in breast cancer treatment will contribute to the next studies for designing target therapy agents and approaches.

Keywords: Breast cancer, Sphingolipid, Solid lipid nanoparticles

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Oral Presentation – 29

Combination Therapy of Beta-Hydroxybutyrate and Oxaliplatin Augments the Treatment Efficacy in Colorectal Cancer Organoids

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Introduction and Aim: Treatments focused on targeting cancer metabolism are a promising option in the battle against colorectal cancer. Beta-hydroxybutyrate (BOHB), serves as a supplier of acetyl-CoA for the Trichloroacetic acid (TCA) cycle and it potentially redirects energy metabolism the cycle. Recently revealed oxaliplatin ‘s mechanism of action was proceeding on reactive oxygen species (ROS) caused apoptotic cell death. This investigation delves into BOHB's potential to enhance the cytotoxic impact of oxaliplatin by shifting energy metabolism into TCA cycle resulting in electron transport chain which is primary sources of ROS.

Materials and Methods: This study was performed on advanced in vitro organoid technology. The combined efficacy of BOHB and oxaliplatin was assessed using a cell viability assay. Western Blot analysis was used to indicate the levels of pivotal proteins involved in energy metabolism, apoptotic pathways, DNA damage, and histone acetylation markers. Flow cytometry was utilized to quantify ROS levels.

Results: BOHB with oxaliplatin elevated the cytotoxic effect on colorectal cancer organoids. Administration of BOHB and/or melatonin yielded noticeable reductions in Lactate Dehydrogenase A and increased Mitochondrial Carrier Protein 2 levels, signifying aerobic glycolysis suppression and augmentation in oxidative phosphorylation rate. This metabolic shift triggered apoptotic cell death through oxaliplatin, attributed to elevated ROS levels. As a positive control, melatonin countered this impact by safeguarding cancer cells against heightened oxidative stress conditions.

Conclusion: These novel combinations hold promise in improving treatment outcomes for individuals afflicted by colorectal cancer. (Tolga Sever was supported by TUBITAK 2211A Domestic Doctoral, 2214 Overseas Doctoral Research and Council of Higher Education 100/2000 Scholarship Programs.)

Keywords: Colorectal cancer, Organoid, Beta-hydroxybutyrate, Oxaliplatin, Reactive oxygen species, Metabolic targeted therapy.

Oral Presentation – 30

Editing the TP53 Gene Locus in U87 Human Glioblastoma Cell Line by Using CRISPR/Cas9 System

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Introduction and Aim: The p53 tumor suppressor is mutant in nearly half of cancer cases. Although the roles of p53 mutations are well-studied, for some cancer types such as glioblastoma, there is still need for comprehensive studies. In this study, we aimed to engineer the *TP53* gene locus in U87 cells to generate a cell line lacking p53 expression for further mutant p53 studies in glioblastoma.

Materials and Methods: We targeted the *TP53* gene locus by using CRISPR/Cas9 system in U87 cells. After evaluation of the gene editing by performing genotyping, we screened the single-cell clones derived from the gene edited cell pool and determined the homozygous knockout clones. We confirmed the edit by Sanger Sequencing and analyzed the p53 protein levels by western blot. To compare WT and p53 knockout U87 cell behaviors, we performed trypan blue exclusion, wound healing and colony formation assays.

Results: We managed to edit the *TP53* gene locus in U87 cells and confirmed the loss of p53 protein expression. Also, we did not observe any off-target effect. By considering proliferation, migration and colony formation abilities of WT and p53 knockout cells, the newly generated cell line was not only genotypically but also phenotypically bearing the p53 knockout profile.

Conclusion: The newly generated cell line can be used as a glioblastoma cell line model for mutant p53 overexpression studies.

Keywords: p53, Glioblastoma, CRISPR/Cas9, U87

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Oral Presentation – 31

Gastric Cancer Spheroids: A Three-Dimensional Model to Study the Effect of Metabolic Alterations in the One-Carbon Pathway

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Introduction and Aim: Cancer cells alter their metabolism compared to healthy cells to survive, proliferate, and metastasize. This leads to high demand for 1C units to successfully complete these processes which are supplied by the one-carbon pathway. Analysis of 1C metabolism and its relation to anti-cancer drug responses requires cell culture models that closely mimic the tumor organization and functionality as observed in vivo such as 3D multicellular tumor spheroids (MCTS). Here, we developed high-throughput gastric MCTS, and characterized their growth and 1C metabolism-related protein levels compared to 2D cultures.

Materials and Methods: We developed MCTS from gastric cancer cell lines, SNU484 and NCI-N87, in 96-well plates by using the liquid overlay technique. We characterized spheroid morphology and growth by imaging, MTT assay, and flow cytometric analysis. Their metabolites were analyzed by NMR, Real-Time qPCR, and western blotting.

Results: We formed compact spheroids with both cell lines with high cell viability during 6 days of culture according to flow and MTT data. NMR data shows high formate levels in both cell lines. qPCR and western blots show changes in the expression levels of 1C metabolism-related proteins such as SFXN1, SHMT1/2, and MTHFD1/2 in spheroids compared to monolayers. Bioinformatic analysis of comprehensive patient datasets revealed that these genes are associated with a poor response to chemotherapy in gastric cancer.

Conclusion: Targeted metabolomics, gene, and protein levels have the potential to indicate altered one-carbon metabolism in our gastric MCTS models which can be useful to investigate drug resistance in gastric cancer.

Keywords: multicellular tumor spheroids, gastric cancer, one-carbon metabolism, drug resistance, formate overflow

Oral Presentation – 32

Regulatory Network of miR-27a-5p in Prostate Cancer

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Introduction and Aim: miR-27a-5p was shown to be significantly downregulated in prostate cancer (PCa) and its forced-overexpression lead to a decrease in the viability of LNCaP cells. Therefore, miR-27a can be considered as a therapeutic target in PCa. The regulatory network of miR-27a-5p and its target genes remain to be clarified. Here, we aimed to reveal the tumor suppressor role of miR-27a-5p by directly targeting CCR5, STAT3, and Bcl-2, all of which are components of chemokine signaling and known to promote PCa progression.

Materials and Methods: CCR5, STAT3, and Bcl-2 were determined as the potential target genes of miR-27a-5p via bioinformatics. Expression levels of miR-27a-5p and its predicted target genes were determined by qRT-PCR in tumor samples of nude PCa mice models, generated with either PC3 or LNCaP cells.

Results: It was found that miR-27a-5p is significantly downregulated, and CCR5 and Bcl-2 gene expression levels were found to be significantly upregulated in all PCa tumors. STAT3 expression was detected only in LNCaP tumors.

Conclusion: We showed that miR-27a-5p expression is inversely correlated with the expression of CCR5 and Bcl-2 genes. These results support the hypothesis of miR-27a-5p directly targeting chemokine signaling components and highlight the therapeutic potential of miR-27a-5p in PCa. To further confirm this regulatory network and tumor suppressive function of miR-27a-5p, in vitro experiments, including gene expression profiles upon mimic/anti-miR transfection will be performed, and the effects on cellular processes will be assessed.

Keywords: miRNA, prostate cancer, chemokine signaling, gene expression

Oral Presentation – 33

Investigation of Apoptotic Potential of Catechol in Drug-Resistant Lung Cancer and Healthy Fibroblast Cells

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Introduction and Aim: Many herbal compounds are applied for phytotherapy purposes in lung cancer (H1299), the incidence of which is increasing globally. However, it is a fact that this compound, which will be used to treat lung cancer, also affects healthy cells. Activation of the apoptotic pathway was investigated to demonstrate the anticancer effect of catechol on drug-resistant lung cancer cells. In addition, the activation of the apoptotic pathway was studied with healthy fibroblast (Bj) cells and the results were compared.

Materials and Methods: The 24-hour cytotoxic effect of catechol on cells was demonstrated by the Cell Titer-Blue® cell viability test. In order to determine the apoptotic potential, the caspase 3/7 activity of the cells exposed to catechol was measured and the potential of catechol to stimulate the apoptotic pathway was determined. Caspase 3/7 enzyme activity was determined using the Promega 'ApoTox-GloTM Triplex Assay' kit.

Results: In our study, the IC50 values of the cytotoxic effect of catechol on drug-resistant lung cancer and healthy fibroblast cells were found to be 90 and 207 µg/ml, respectively. Caspase-3/7 activity in drug-resistant lung cancer and Bj cells increased 2.3-fold and 1.6-fold, respectively, compared to control after 24 hours of catechol incubation.

Conclusion: In conclusion, drug-resistant lung cancer cells have higher caspase 3 activity than healthy cells, indicating that catechol has a higher apoptotic potential in drug-resistant cancer cells than healthy cells.

Keywords: Catechol, Drug-resistant, Apoptosis

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Oral Presentation – 34

Epigenetic Changes/ DNA methylation plays a key role in Triple Negative Breast Cancer?

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Introduction and Aim: Breast cancer is among the most common cancers in women in the world and is the second leading cause of cancer-related deaths. Triple negative breast cancer (TNBC) is a subgroup of breast cancer in which estrogen (ER), progesterone (PR) and HER2 receptors are not expressed. It is aimed to demonstrate the usability of DNA Methylation profiles, which is one of the epigenetic changes of SFRP1 (Secret Frizzled Related Protein-1) in a selected tumor suppressor gene, as biomarkers in TNBC patients.

Materials and Methods: In the literature studies on the SFRP1 gene, it was observed that there was no extensive methylation study in the TNBC subtype. DNA isolation was performed from the tissue (paraffinized) of 110 patients diagnosed with TNBC. After bisulfite modification, methylation states were determined using MSP-PCR. Finally, it was visualized by running on agarose gel. The methylation results and demographic characteristics of the patients were evaluated using the SPSS program.

Results Conclusion: As a result of the studies, it was observed that the SFRP1 gene was methylated in almost all of the patients. Gene methylation are thought to be effective in gene silencing in TNBC patients.

Conclusion: The emergence of results in parallel with the literature studies is important for the continuity and elaboration of the study.

Keywords: Epigenetic, Methylation, TNBC

Oral Presentation – 35

Synergistic Anticancer Effects of Auraptene and Tamoxifen on MCF-7 and Ishikawa Cell Cultures in Breast and Endometrial Cancer Cell Lines

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Introduction and Aim: Since breast cancers express high estrogen receptors the use of selective estrogen receptor modulator Tamoxifen is common in the treatment. Tamoxifen increases the risk of endometrial cancer. We planned to examine the possibility of cytotoxicity of the monoterpene coumarin compound Auraptene, which has been shown to have an antiproliferative effect in breast cancer cells, in estrogen-dependent endometrial cancer modeling by Ishikawa cells. No study was found in the literature showing the cytotoxicity of Aurapten against Ishikawa cells and endometrial cancer. We studied the potential of Auraptene combined with Tamoxifen in suppressing the endometrial carcinogenesis induced by Tamoxifen and attaining a synergistic effect in breast cancer therapy.

Materials and Methods: Single and combined doses of Auraptene and Tamoxifen were administered to human breast and endometrial cancer cell lines MCF-7 and Ishikawa cell cultures passaged from cell culture laboratory stocks. Cell viability and proliferation were quantified by WST-8 assay with a Multiscan ELISA microreader. Apoptosis assays with the Annexin V/PI staining method and cell cycle tests were analysed with flow cytometry. Cells and nuclear morphology were visualized by laser scanning confocal microscope.

Results: Auraptene elicited cytotoxic effects in Ishikawa and MCF-7 cells by increasing apoptosis and inducing their arrest in the G0/G1 phase of the cell cycle ($p<0.001$). Tamoxifen incited the proliferation in Ishikawa cells however this stimulation was curbed when combined with Auraptene.

Conclusion: Auraptene can be recommended as a synergistic therapeutic adjuvant in breast cancer to enable Tamoxifen to use more safely by reducing the risk of endometrial cancer and effectively at lower doses.

Keywords: Auraptene, Tamoxifen, breast cancer, flow cytometry, cytotoxicity.

Oral Presentation – 36

Determination of Antioxidant Properties and Contents of Helichrysum Arenarium L. Extracts, Investigation of Anti-growth Effects Against Human Breast Cancer Cell Lines

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Introduction and Aim: H. arenarium (dwarf everlast or immortelle) is used in the treatment of various diseases. In addition, scientific studies show that H. arenarium is a rich source of antioxidants. Natural antioxidants are known to have many positive biological activities. This study aims to determine the most efficient solvent in the extraction of H. arenarium using solvents with different polarities, to reveal its antioxidant properties, to determine the its active ingredients and growth inhibitory effects against MCF-7 and MDA-MB-231 human breast cancer cells.

Materials and Methods: Ultrasonic extractions of H. arenarium were performed with four different solvents: hexane, acetone, ethanol and glycerol-water. The total phenolic content and antioxidant capacity of the extracts were determined by spectrophotometric methods, and the quantitative analysis of the phenolic components was carried out by HPLC-DAD. The extracts were lyophilized and dissolved with DMSO. Then, the MCF-7 and MDA-MB-231 cell lines were treated at a final concentration of 0.1-1000 µg/mL and their viability was assessed by using sulforhodamine B viability assay.

Results and Conclusion: The highest total phenolic content and antioxidant capacity among four different solvents was observed in the extract prepared with glycerol-water solvent mixture. When the HPLC-DAD results were examined, the highest amount of phenolic component contained in the extracts was determined as kaempferol-3-β-D-glycoside. All extracts of H. arenarium significantly inhibited the growth of both cell lines in a concentration-dependent manner. The effects of H. arenarium extracts in combination different chemotherapeutic agents or against different cancer cell lines can be studied in the future to better elucidate its anti-growth properties.

Keywords: Breast cancer, Antioxidant, HPLC-DAD, Helichrysum Arenarium L., MCF-7, MDA-MB-231.

Oral Presentation – 37

The Anticancer Potential of Brassinin in Estrogen Receptor-Positive Breast Cancer Cells Through The Activation of Apoptosis and Downregulation of Matrix Metalloproteinase-2

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Introduction and Aim: Matrix metalloproteinases (MMPs) are a family of proteolytic enzymes that are responsible of tissue remodelling. Overexpressed MMPs are known to play a crucial role in cancer invasion and metastasis. Therefore, suppression of these enzymes is particularly important in cancer treatments. Brassinin is an indole derivative of a family of natural compounds known as phytoalexins. They exert antimicrobial and antioxidant activities. However, it has been reported that brassinin exhibits potent antiproliferative effects in several cancers. In the present study, the cytotoxic and apoptotic effects of brassinin were investigated in estrogen receptor-positive breast cancer cells. Additionally, the suppressive impact of the compound on MMP2 activity was examined.

Materials and Methods: The cytotoxic effects of brassinin on breast cancer cells was determined by MTT and cell cycle assays. The apoptotic activity of the compound was investigated by annexin V binding assay. The activity of MMP2 was detected by ELISA.

Results: The results revealed that brassinin decreases cell viability significantly at 200 µM and causes cell cycle arrest at S phase in all applied concentrations. Furthermore, it has been observed that brassinin significantly increases apoptotic cell population and suppresses MMP2 activity.

Conclusion: In conclusion, the present study demonstrated that brassinin exhibits significant anticancer activity on estrogen receptor-positive breast cancer cells via leading to apoptosis and downregulating the activity of MMP2.

Keywords: Brassinin, breast cancer, MMP2, phytoalexins.

Oral Presentation – 38

Unveiling Potential: Scorpio fuscus Venom for Targeted Colorectal Carcinoma Therapy

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Introduction and Aim: Colorectal carcinoma (CRC) is a significant cancer-related cause of death. This study extensively characterizes *Scorpio fuscus* venom, identifies potent peptides/proteins, models their structures, evaluates *in vitro* effects on CRC cells, and investigates *in vivo* impact using a mouse model.

Materials and Methods: Utilizing a tandem approach of 2D gel electrophoresis and high-resolution mass spectrometry, we identified *S.fuscus* venom constituents. The ensuing peptides underwent rigorous scrutiny, including three-dimensional modeling and docking with pivotal proteins in colon cancer and apoptosis pathways. The venom's impact on colorectal carcinoma cell lines(DLD-1, HT-29, CaCo-2, CCD-18Co) was meticulously assessed, spanning cytotoxicity, migratory behavior, colony-forming, and apoptosis, quantified via advanced flow cytometry. Detailed mRNA and protein cascade changes in apoptosis and CRC were illuminated through pathway panels. An orthotopic colon cancer model in male non-scid mice facilitated an in-depth evaluation of the venom's *in vivo* tumor developmental effects.

Results: Proteomic exploration unveiled 18 distinct bioactive peptides in *S.fuscus* venom. In colon cancer cells, dose-dependent cytotoxicity exhibited IC50 values of 14.8 µg/mL(DLD-1) and >250 µg/mL(CCD-18Co). Remarkable inhibition emerged, with 84% metastasis reduction and 49% colony formation decline. Strikingly, BAK1 and TRAF3 mRNA plummeted tenfold, while BIRC2-3-6, CASP8, TNFRSF8-11, and BOK surged tenfold. Intratumoral venom reduced primary tumor volume by 30%, with no metastatic loci, emphasizing potential therapeutic value.

Conclusion: Intriguingly, *Scorpio fuscus* venom's bioactive peptides exhibit dose-dependent cytotoxicity, hinder metastasis, and modulate crucial genes, suggesting potential for targeted CRC therapy.

Keywords: *Scorpio fuscus*, Colorectal carcinoma, Proteomics, Apoptotic pathway, Cytotoxicity

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Oral Presentation – 39

Enhanced cytokine stimulation in in vitro and in vivo glioblastoma models: Lipid nanoparticles for stimulator of interferon genes agonists delivery

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Introduction and Aim: The most common brain tumour in adults, Glioblastoma (GBM) is still considered incurable. Researchers are in a continuous search for an efficient therapeutic strategy. Natural and synthetic cyclic dinucleotides (CDNs) and non-nucleic acid agonists of the stimulator of interferon genes (STING) demonstrated huge potential for cancer treatment and entered clinical studies. However, these have disadvantages such as low solubility, and adverse effects related to excessive cytokine release upon systemic administration. The aim of this study was to develop diABZI-loaded lipid nanoparticles (LNPs) to be used as an intranasal treatment against GBM.

Materials and Methods: LNPs loaded with a lipophilic non-nucleotide STING agonist, diABZI were prepared by lyophilisation-rehydration-sonication method. Nanoparticles were evaluated in terms of physicochemical characteristics and cytotoxicity on L929 and GL261 cell lines. Cellular uptake was evaluated on GL261 cell line. Cytokine stimulation activity was assessed on THP1 monocytes *in vitro* and in an orthotopic syngeneic mouse tumour model after IV and IN application.

Results: PEGylated cationic LNPs with particle size <250 nm and drug entrapment efficiency over 99% were obtained. No significant cytotoxicity was observed. Higher cellular uptake was observed with cationic nanoparticles. *In vitro* and *in vivo* studies revealed higher cytokine stimulation and improved healing after IN and IV application of diABZI LNPs.

Conclusion: diABZI LNPs had high cytokine stimulating activity *in vitro* and *in vivo* and demonstrated good *in vivo* performance when applied as a single treatment. Further research is needed to examine the kinetic profile of the cytokine stimulation after treatment.

Keywords: diamidobenzimidazole compound 3, lipid nanoparticles, nanomedicine, immunostimulation, nose-to-brain delivery, STING agonists

This study is supported by the Health Institutes of Türkiye (TÜSEB, Project #4469)

Oral Presentation – 40

Investigation of anticancer activity of mocetinostat (Hdaci) on MDA-MB-231 breast cancer cell line

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Introduction and Aim: HDACi (histone deacetylase İnhibitors) stop the cell cycle, induce apoptosis and inhibit angiogenesis are recognised as important agents in the treatment of cancer. Mocetinostat (MGCD0103) is one of the members of Class I Histone Deacetylase Inhibitors (HDACi) and its mechanism of action has not been defined, yet in cancer researches. The aim of the study is ınvestigation of anticancer activity of mocetinostat on MDA-MB-231 breast cancer cell line.

Materials and Methods: The effects of mocetinostat on MDA-MB-231 breast cancer cells were investigated by cell viability, migration assays and ros sssay technique.

Results: The concentrations of drug that give a half-maximal response (IC_{50}) were detected for mocetinostat (5µM) for 48 hr. We observed that cell migration decreased, DNA fragmentation increased compared to the control group. ROS generation in breast cancer cells was increased due to mocetinostat exposure.

Conclusion: Mocetinostat played a role through inducing apoptosis on breast cancer cells in a time.

Keywords: MDA-MB-231, Breast cancer cell, Mocetinostat

Oral Presentation – 41

Investigation of Anti-Cancer Effects of a Palladium Complex (Pd(bpma)(barb).Cl • H2O) in Ovarian Cancer Cell Lines

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Introduction and Aim: Chemotheraphy for ovarian cancer relies on cisplatin and carbolaplatin which are highly prone to cause therapy resistance. The palladium compexes gather great interest since they constitute a more stable and soluble structure compared to platinum isostruchers. The main objective of this study is to investigate anti-cancer activity of a palladium complex (Pd(bpma)(barb).Cl • H_2O) in ovarian cancer cell lines and to explain the possible mechanism behind it.

Materials and Methods: The anti-cancer potency of the palladium complex was investigated in varying doses from 1 nM up to 100µM for 48 hours by using MTT assay in three different high grade serous ovarian cancer cell lines; CaOv-3, Kuramochi, Ovsaho. The mechanism of cell death were analyzed with fluorescent staining and flow cytometry. Scratch assay were used for quantification of migration rate.

Results: Palladium complex was found to be effective on all cell lines espacially on Ovsaho with 13µM IC_{50} which is comparable to that of cisplatin while the migration were inhibited espacially on CaOv-3. The complex causes the apoptotic cell death trigered by DNA damage and oxidative stress.

Conclusion: The palladium complex is a promissing anti-cancer agent for the treatment of a particular sub-class of ovarian cancer.

Keywords: palladium, ovarian cacer, anti-cancer

Oral Presentation – 42

Comparison of the Effect of Abemaciclib in MCF-7 Cells in 2D and 3D Systems

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Introduction and Aim: Breast cancer represents a prominent global oncological challenge. Three-dimensional (3D) models have been proven superior to two-dimensional (2D) systems in recapitulating *in vivo* conditions. We evaluated the anti-tumor efficacy of Abemaciclib, an active constituent of Verzenio, against human breast cancer cells (MCF-7) cultivated in 2D and 3D models for hormone receptor-positive (HR+) advanced breast cancer.

Material and Method: The half-maximal inhibitory concentration (IC_{50}) of Abemaciclib on MCF-7 cells in 2D cultures was ascertained via the 3-(4,5-dimethylthiazol-2-yl)-5-(3-carboxymethoxyphenyl)-2-(4-sulfophenyl)-2H-tetrazolium (MTS) assay. Subsequently, MCF-7 cells were cultured in 3D Petri Dish® plates, and spheroid diameter/area were quantified over 6 days. The responsiveness of the spheroids to Abemaciclib, according to the determined IC_{50}, was analyzed using MTS. CellTracker immunofluorescent dyes illustrated cellular localizations in both systems.

Conclusion: MCF-7 cells formed spheroids within 72 hours in a medium containing 10% FBS, accompanied by a decrease in diameter/area. Comparative analysis of 2D and 3D viability revealed anti-cancer properties at specific concentrations in the 2D system, whereas the 3D system exhibited no corresponding decline in cell viability, and indeed, the number of viable cells increased at the same concentration.

Argument: 3D Petri Dish® models demonstrate suitability for soft tissue modeling, such as breast cancer. Our findings underscore that 3D MCF-7 spheroids exhibit enhanced resistance to Abemaciclib in comparison to 2D models, thereby closely mimicking *in vivo* conditions.

Keywords: 3D Petri Dish, MCF-7, Abemaciclib, MTS Analysis, Cell Tracker Staining

This work was financially supported by the Scientific and Technical Research Council of Turkey (Application No: 1919B012224314).

Oral Presentation – 43

Anticancer effect of Tricholoma atrosquamosum Sacc. against human lung adenocarcinoma cell line

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Introduction and Aim: Mushrooms have been collected from nature and consumed since ancient times. Due to their rich nutritional content, they are considered functional foods that are beneficial for health. For this reason, they have been used for many years for medicinal purposes. Thanks to the bioactive components they have, they are known to have antimicrobial, antioxidant, anti-inflammatory, immunomodulatory, and anticancer effects. *Tricholoma* sp. are edible and medicinally important mushrooms. Among these species, *Tricholoma atrosquamosum* Sacc., known as the scaly blackgirl fungus, is a mushroom species with medical importance in the geography of our country. This species is found in the Central and Eastern Black Sea Region, Adana, Siirt, and Kahramanmaraş regions in our country where there are coniferous trees. In this study, it was aimed to determine the cytotoxic effect of ethanol extract of *T. atrosquamosum* at different concentrations (62.5-1000µg/mL) against A549 cells in 24 and 48 hours.

Material and Methods: 3-(4,5dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide method was used to determine the cytotoxic effect.

Results: In the results obtained, the IC_{50} value at the 24th hour was 54.449 µg/mL, while the IC_{50} value at the 48th hour was determined as 99.447 µg/mL.

Conclusion: These results show that *T. atrosquamosum* ethanol extract has a cytotoxic effect depending on increasing concentrations.

Keywords: Medicinal mushroom, *Tricholoma atrosquamosum*, Cytotoxic effect.

Oral Presentation – 44

TFEB Drives Chemo-Immuno-Resistance In Lung Cancer

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Introduction and Aim: Transcription factor EB (TFEB) is a leucine zipper protein and a major regulator of lysosomal biogenesis and autophagy. These two events confer chemoresistance in solid tumors, by sequestrating chemotherapeutic drugs, and also modulate the immune-recognition. In this study, we investigated if TFEB affects the response to chemotherapy and to Vγ9δ2 T-lymphocytes in non-small cell lung cancer (NSCLC).

Materials and Methods: Changes in the expression of TFEB and ABC transporters and their effect on survival in NSCLC were analyzed by using the TCGA-LUAD dataset. TFEB was silenced in H441 and H2228 cells. Metabolic associated pathways were measured by RT-PCR, immunoblotting, and radiolabeling. Co-cultures between NSCLC cells and γδ T-lymphocytes were set-up to measure their expansion and cell killing. Wild-type (WT) and shTFEB NSCLC xenografts implanted in Hu-CD34^{+} NSG mice were used for in vivo validation.

Results: TFEB^{high}ABCA1^{high}ABCC1^{low} phenotype is associated with overall survival. By reducing the pERK1/2-SREBP2 axis that modulates genes of cholesterol homeostasis, TFEB silencing decreased expression and activity of the cholesterol/IPP transporter ABCA1, the efflux of IPP, and the NSCLC killing by γδ T-lymphocytes. shTFEB NSCLC xenografts implanted in Hu-CD34+ NSG mice, were resistant to cisplatin, but were resensitized by zoledronic acid, which re-activates γδ T-lymphocytes killing and down- regulates ABCB1/ABCC1.

Conclusion: We propose TFEB as a driver of chemo-immuno-resistance in NSCLC. Future experiments including a tumor single-cell transcriptomic profile are clarifying which cell populations and pathways make TFEB a controller of chemo-immuno-resistance in NSCLC. Supported by the AIRC (Grant No. IG21408).

Keywords: TFEB, ABCA1, ABCB1, ABCC1, NSCLC, Zoledronic Acid

Oral Presentation – 45

Long Non-Coding RNA Urothelial Carcinoma-Associated 1 Regulates Proliferation And Migration in Doxorubicin Resistance of Estrogen Receptor Positive Breast Cancer Cells

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Introduction and Aim: Breast cancer is the most frequently diagnosed cancer in women and doxorubicin is common used chemotherapy drug in the treatment of many cancer types including metastatic breast cancer. Cancer cells with a negative response to the treatment of doxorubicin trigger drug resistance. Urothelial carcinoma-associated 1 (UCA1) is long non-coding RNA (lncRNA), known to be overexpressed in breast tumorigenesis, but its role in chemotherapy resistance is largely unknown. The aim of this study was to investigate the role of UCA1 in proliferation and cell motility in doxorubicin resistance MCF-7 cell line.

Materials and Methods: Previously developed doxorubicin resistant MCF-7 cells (MCF-7/Dox) up to 640 nM were used. In order to transfect small interfering RNAs (siRNAs) specifically targeting lncRNA UCA1 purchased from Ambion (USA), LipofectMax (A.B.T Biosciences, Turkey) protocol was used according to the modified manufacturer's instructions. At 48 h after transfection, the cells were used to analyze cell viability and wound healing assay.

Results: According to MTT results, the inhibition concentration (IC_{50}) value of doxorubicin in MCF-7/Dox cells was determined as 128.5 µM. UCA1 silencing was confirmed by qRT-PCR. After UCA1 silencing, it was determined that the IC_{50} value of doxorubicin on MCF-7/Dox cells as 88.5 µM. Finally, the cell motility decreased after silencing the UCA1 gene in MCF-7/Dox cell line.

Conclusion: It could be concluded that UCA1 partially reversed doxorubicin resistance by regulation of cell proliferation and motility.

Keywords: MCF-7 cell line, doxorubicin, UCA1

Oral Presentation – 46

Predicting side-effects of chemotherapeutic agents through analysis of drug-induced transcriptomic response

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Introduction and Aim: Among the most common side effects induced by chemotherapy are alopecia, edema, and diarrhea, although their severity depends on the drug, dosage of the drug, and frequency of the treatment. While there exists proposed mechanisms by which anticancer agents cause these side effects, the exact underlying mechanisms have not been entirely clarified. Our aim was twofold: to develop a model that uses drug-induced transcriptome response to predict side effects accurately and to explain the mechanism of the side effects of interest.

Materials and Methods: The selection of drugs was carried out based on the side effect information, collected from SIDER database. Induced transcriptome responses for the selected drugs were obtained from LINCS L1000 project. We trained several classifiers using random forest with iterative feature selection. We used the side effects of interest as class labels and a pool of differentially expressed genes as features. We employed several performance metrics to select the optimal model.

Results: Our approach revealed an expressionsignatures involving 40 genes, which accurately predicted side effects of interests with an 89% accuracy. Out of 40 signature genes 27 were associated to at least one of the side effects by previous studies. The resulting gene signature was further investigated, and its relation to the side effects was explored through functional enrichment analysis and protein-protein interaction networks.

Conclusion: In this study, we developed a model based on random forest algorithm to accurately predict the widely occurring side effects of chemotherapy. The approach that we employed here can be generalized to other side effects.

Keywords: side-effects, chemotherapeutic agents, random forest

Oral Presentation – 47

The Impact of 1.25-Dihydroxyvitamin D3 on Mitophagy and Apoptotic Pathways in Hepatocellular Carcinoma

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Introduction and Aim: 1.25-dihydroxyvitamin D3 is the active form of vitamin D which effects the cellular mechanisms directly. Mitophagy is a type of autophagic mechanism that aids in cellular recycling by consuming unhealthy or damaged mitochondria. In this study, we aimed to know how 1,25-dihydroxyvitamin D3 affected the apoptotic and mitophagy pathways in hepatocellular carcinoma (HCC) cells.

Materials and Methods: Total RNA was isolated after 48 hours of treatment with 250 nM 1,25-dihydroxyvitamin D3 on HepG2 cells. By using RT-PCR, isolated total RNAs were used to identify the gene expressions of MFN1, MFN2, Parkin, and PINK1 genes for mitophagy, as well as Cyt C and p53 for apoptosis.

Results: MFN1, p53 and Cyt C gene expressions were downregulated following a 250 nM 1.25-dihydroxyvitamin D3 treatment at the 48th hour in comparison to the control group ($p<0.001$). Despite the decrease in Parkin gene expression, no statistical difference was observed ($p>0.05$). In comparison to the control group, statistically significant increases in MFN2 and PINK1 gene expressions were observed ($p<0.001$).

Conclusion: By promoting mitophagy, 1,25-dihydroxyvitamin D3 helps HepG2 hepatocellular carcinoma cells to prevent apoptosis. Although some researchers suggest that 1,25-dihydroxyvitamin D3 has anti-carcinogenic and preventive characteristics, a growing number suggest that tumor cells can have aggressive behavior following HCC. 1,25-Dihydroxyvitamin D3 was not recommended for the treatment of HCC in our previous research. Based on the obtained data from this study, we continue to support the same hypothesis.

Keywords: 1.25-dihydroxyvitamin D, Apoptosis, Hepatocellular Carcinoma, Mitophagy

Oral Presentation – 48

Combination Therapy of dual PI3K/mTOR Inhibitor and Curcumin shows anticancer effect on Colorectal Cancer

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Introduction and Aim: Colorectal cancer is a heterogeneous disease that is highly diagnosed worldwide. Curcumin is an anticancer agent that is effective in colorectal cancer. However, poor chemical stability of curcumin limit its antitumor activity in clinical applications. PI3K/AKT pathway plays an important role in the aggressive nature of cancer including resistance to chemotherapy. NVP-BEZ235 is a dual PI3K/mTOR kinase inhibitor that induces apoptosis and suppresses the growth of cancer. The current study investigates the synergetic anticancer effect of NVP-BEZ235 and curcumin on colorectal cancer.

Materials and Methods: MTS assay was conducted to detect the cytotoxic effects of curcumin and NVP-BEZ235. Cellular uptake was determined by flow cytometry. Colony forming assay was investigated the growth inhibition of HCT116 cells. Cell cycle, Annexin V/PI and gene expression levels were evaluated to determine the anticancer effect.

Results: Synergistic effect was seen in combination treatment of curcumin and NVP-BEZ235 in HCT116 cells. Cytotoxicity of both anticancer agents was observed in a dose and time dependent manner. Colony forming assay reveals that combination therapy of curcumin and NVP-BEZ235 can inhibit the growth of HCT116 cells. Cell cycle arrest at SubG0 phase shows improved anti-cancer characteristics. Annexin V/PI assay showed increase in early and late apoptosis in combination group when compared to control group. Moreover, qPCR results showed significant increase in the apoptosis related gene expression levels.

Conclusion: Taken together, our findings demonstrate that combination therapy of NVP-BEZ235 and curcumin has anticancer potential in HCT116 cells. These anticancer agents together may be a promising therapeutic candidate for colorectal cancer therapy.

Keywords: NVP-BEZ235, curcumin, synergistic effect, anti-cancer effect, colorectal cancer

Oral Presentation – 49

The role of Trop-2 expression in determining the effectiveness of Sacituzumab Govitecan in the treatment of triple-negative breast cancer patients.

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Introduction and Aim: Triple negative breast cancer (TNBC) is the most aggressive of all breast cancer subtypes. In recent years, antibody-drug conjugate based therapies developed for TNBC have shown promising results. Sacituzumab govitecan (SG), is an anti-Trop-2 antibody-drug conjugate with SN-38, which was approved by the FDA in 2020. In our study, we aimed to evaluate the expression of Trop-2/Tacstd2 in TNBC patients to determine who would benefit from SG treatment and, in addition, to evaluate the significance of clinical parameters associated with the Trop-2 expression data obtained in these patients.

Materials and Methods: In this study, RNA was isolated from 45 paraffin-embedded tumors and normal tissues, and then cDNA synthesis was performed. Trop-2 expression levels were investigated using the RT-PCR method. Quantitative data obtained were evaluated using normality tests, t-tests, X^2-tests and correlation analysis.

Results: The gene expression differences between tumor and normal tissues of the patients were analyzed. A 1,935-fold increase in Trop-2 expression (p=0,033) was observed. When the expression differences obtained were evaluated together with the clinicopathological data of the patients, statistical significances was determined between the Trop-2 expression difference and necrosis (p=0,041), in-situ component (p=0,037) and pathological tumor size (p=0,035).

Conclusion: It is crucial to elucidate the differences in Trop2 expression (increased or decreased expression) in specific cancer types and disease stages in order to unveil the full role of Trop2 in cancer growth and metastasis. Our findings provide crucial clues for the first time regarding the role of Trop-2 as a prognostic biomarker in TNBC.

Keywords: Breast Cancer, TNBC, Sacituzumab Govitecan, SN-38 Trop-2

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Oral Presentation – 50

Investigation of the Relationship Between Bivalent Promotor Regions And Epithelial-Mesenchymal Cancer Cells Plasticity

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Introduction and Aim: Cell plasticity contributes to transition across distinct cell states by epithelial-mesenchymal transition (EMT) and vice versa. It enables to acquire phenotypic and functional features of pathological conditions during tumor progression. The dynamism points to epigenetic regulation such as "Bivalent promoter" regions which are simultaneously marked by both activating H3K4me3 and repressive H3K27me3 modifications. The aim of our study was to investigate bivalency and changes in "bivalent promoter" regions of genes including stem cell markers, differentiation markers and polycomb group members.

Materials and Methods: To mimic cancer cell plasticity, HT-29 cells which undergo spontaneous MET/EMT, were used. Three cell population were generated: parental (pHT-29), epithelial (eHT-29) and mesenchymal (mHT-29) cells. The chromatin domains containing both H3K4me3 and H3K27me3 were immunoprecipitated by sequential chromatin immunoprecipitation and the bivalency in the promoters of stem cell markers (CD44 and CD133), differentiation and epithelial marker (CDX2), and polycomb group members (CBX4, CBX7 and CBX8) as well as expression levels were determined by qPCR.

Results: Bivalent marks in CD133 and CD44 promoters were found at higher levels in mesenchymal cancer cells in line with increased gene expression. Similar bivalency in CDX2 promoter regions were seen in mHT-29 cells with decreased CDX2 mRNA levels. Also, for CBX4, CBX7 and CBX8, bivalency was determined in mesenchymal cells. While CBX7 and CBX4 mRNA decreased, CBX8 mRNA increased in mHT-29 cells.

Conclusion: The effect of bivalent promoters on the plasticity of cancer cells has not been fully explained. The results showed that mesenchymal cancer cells had bivalent promoter marks in line with stem cell phenotype.

Keywords: colon cancer, cancer plasticity, epithelial-mesenchymal transition, mesenchymal-epithelial transition, epigenetic regulation, bivalent promotor.

Oral Presentation – 51

Ceramide Binds Smad7 to Regulate Solid Tumor Metastasis

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Introduction and Aim: Although the cancer survival rate has been significantly improved during the past several years, progress in the treatment of cancer metastasis has been limited. Therefore, development of mechanism-based novel therapeutic strategies for targeting cancer metastasis is urgently needed. Thus, in this study we aimed to determine the structural details of how CerS4-generated C18-ceramide binds Smad7 for the regulation of TßR-Smo-mediated cancer cell invasion/migration.

Materials and Methods: Interactive docking prediction of protein-lipid complexes and modeling between ceramide and Smad7 were performed using ZDOCK and Phyre2. Ceramide-Smad7 interaction was analyzed with IP and PLA assay. P-Smo protein abundance was detected by immunohistochemistry using anti-P-Smo (S615)-specific antibody.

Results: Our in vitro lipid-protein binding studies showed that recombinant human Smad7 bound ceramide with Kd= 382 nM, which is within its physiological range. Our molecular modeling/simulation study showed that Q300 of Smad7 might be involved in ceramide binding. Ectopic expression of wt-Smad7 highly associated with ceramide, but not mut-Smad7 in PLA assay. We then examined the phosphorylation of Smo in response to CerS4 knockdown. Data showed that CerS4 knockdown resulted in 4.5-fold increase in P-Smo expression compared to controls without affecting total Smo abundance. These data were also consistent with overexpression of P-Smo measured by IHC in metastatic NSCLC compared to non-metastatic tumors using a TMA.

Conclusion: Overall, these data indicate that ceramide might stabilize Smad7 inhibitory complex by directly binding to Smad7 via lipid-protein interaction. Besides, CerS4 knockdown enhances Smo dependent cell migration by inducing Smo phosphorylation at S615.

Keywords: Metastasis, Ceramide, Smad-7, P-Smo

Oral Presentation – 52

A Novel Palladium (II) Complex Selectively Induces Cell Death and Cell Cycle Arrest in Metastatic Colon Cancer Cells

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Introduction and Aim: Colon cancer is the third most common type of cancer in the world. A large number of drugs are used in the treatment of colon cancer, but these drugs are not very effective in late stages of colon cancer. it is difficult to develop an effective treatment and new approaches are needed. Drugs should be effective on cancer cells with low doses, on the other hand they need to show low cytotoxicity on normal cells. In this study, we tested anticancer effects of 4 different new synthesized Pyridine derivative complexes that containing palladium on the SW620 colon cancer cell line and CCD-18CO normal colon cells.

Materials and Methods: First, cell lines were treated with those at ranged concentrations from 1 to 200 µm and IC50 values were calculated by performing cell vitality tests. To evaluated anti-cancer effects of those drugs, we analyzed levels of apoptosis and cell cycle upon to drug treatment. Then, we tested many marker proteins for apoptosis, cell cycle and autophagy with Westernblot.

Results: We observed that one of new synthesis drugs was the most effective at low doses on SW620 and but high doses on CCD-18Co. In addition, a novel palladium (II) complex selectively induced cell death and cell cycle arrest in SW620 cells at low concentration.

Conclusion: In conclusion, we found out that palladium (II) complex has a high potential for new colon cancer targeting therapy. However, future work will be required to observe effect of this new drug in vivo.

Keywords: Colon cancer, palladium (II) complex, apoptosis, cell cycle

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Oral Presentation – 53

Neuroblastoma Targeted Anti-Cancer Drug Delivery

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Introduction and Aim: Everolimus is mTOR inhibitor and Tozasertib is an AURORA inhibitor. Both of these proteins plays an important role in stabilizing MYCN protein. MYCN is an important prognostic marker of neuroblastoma (NB). Ganglioside2 (GD2) is a protein that is overexpressed in tumor tissue in primary NB. Drug delivery systems that directly target tumor cells is an effective method for presenting drug combinations together. In this study effect of the GD2 targeted nanodrug including Everolimus+Tozasertib on NB was studied.

Materials and Methods: 20 mg of PEG-b-PLGA was used to form nanoparticle. IC_{50} doses of therapeutics were added to the nanostructure with 1:3 rate. FTIR, size, loading capacity (LC) and zeta potential were measured. 500 µg of DTX-B (mAb) was attached to target the formed nanoparticle. LC was determined by BCA assay. Xenographt model was formed by injecting Kelly cells. After tumor was formed, IC_{50} doses of nanoparticles per day administered to mice intravenously for 5 days. After treatment and sacrification, tissues were collected. Molecular analyses was performed.

Results: 7.8 mg of EVER-TOZA@PEGbPLGA/DTX-B, showed 30% viability on cells after 24 hours. A reduction in tumor size was observed in mice treated for 5 days. Compared to combination group without NP, EVER-TOZA@PEGbPLGA/DTX-B was effective. Additionally, nanostructure affected on tumor size compared to control. There was a decrease in MYCN and Aurora A gene expression.

Conclusion: Everolimus+Tozasertib combination targeted by nanostructure via GD2 antibody is shown to be a candidate therapeutic agent both in vitro and in vivo animal models in NB.

Keywords: Neuroblastoma, Nanoparticle, Drug Delivery

Oral Presentation – 54

Anti-growth, Antioxidant, and Hepatoprotective Properties of Spirulina platensis Extract

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Introduction and Aim: *Spirulina platensis*, a filamentous cyanobacterium often referred to as blue-green algae, is recognized for its biological activities, including antioxidant, immunomodulatory, anti-inflammatory properties. This study was conducted to investigate the growth inhibitory effects of the ethanolic extract of *Spirulina platensis* on PANC-1 and MIA PaCa-2 human pancreatic cancer cell lines. Additionally, the *in vivo* hepatoprotective, antioxidant properties of *S. platensis* were explored.

Materials and Methods: The ethanolic extract of *S. platensis* was lyophilized and then dissolved in DMSO. Subsequently, PANC-1, MIA PaCa-2 cell lines were treated with concentrations ranging from 0.1 to 1000 µg/ml. Cell viability was assessed using the sulforhodamine B viability assay. For *in vivo* evaluations of hepatoprotective and antioxidant properties, *Spirulina* was administered to rats via gavage at a dose of 500 mg/kg/day for four weeks. The activity levels of superoxide dismutase (SOD), glutathione peroxidase (GSH-Px), alanine aminotransferase (ALT), and aspartate aminotransferase (AST) were measured in the heart and liver tissues of the rats.

Conclusion: The control group that received *Spirulina* demonstrated a significant elevation in the activity of SOD, GSH-Px enzymes in heart and liver tissues. There was a significant reduction in ALT and AST enzyme levels. The extract notably hindered the growth of both examined cell lines. Future research can focus on studying the effects of *Spirulina platensis* extracts in conjunction with various chemotherapeutic agents or its impact on different cancer cell lines to more comprehensively understand its anti-growth attributes.

Keywords: *Spirulina platensis*, Pancreatic cancer, PANC-1, MIA PaCa-2, SOD, GSH-Px.

Oral Presentation – 55

Investigation of the effect of toluene on nitric oxide production and protective properties of resveratrol

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Introduction and Aim: Toluene is one of the most used organic solvents in the world. Prolonged exposure to toluene, causes serious health problems. The International Agency for Research on Cancer (IARC) has classified toluene as "possibly carcinogenic to humans" (Group 2B). This classification states that toluene may have potential carcinogenic effects. Toluene exposure has been linked to the formation of reactive oxygen species and reactive nitrogen species, resulting in direct tissue damage and alteration of various antioxidant systems. Resveratrol is a naturally occurring polyphenol in many plant species known for its diverse biological effect. In this study, the effect of exposure to toluene on nitric oxide production, which has an important role as a biological regulator in cardiovascular, neurological, immunological and many other systems, and the protective properties of resveratrol were investigated.

Materials and Methods: Wistar-Albino male rats weighing 250-350g were administered toluene at a dose of 900mg/kg and three doses of resveratrol (5mg/kg, 10mg/kg, and 20mg/kg) intraperitoneally for six days. Nitric oxide levels and Nitric oxide synthase activities were investigated in liver tissue and serum.

Results: The results showed an increased nitric oxide level in the liver tissue and serum and a high nitric oxide synthase activity following toluene administration. Significant reductions in nitric oxide levels and nitric oxide synthase activity in the liver were observed after the administration of various dosages of resveratrol.

Conclusion: Our results suggested that high doses of toluene induce nitric oxide production, whereas resveratrol possesses protective properties.

Keywords: Toluene, resveratrol, nitric oxide, nitric oxide synthase

Oral Presentation – 56

Investigation of Anti-Cancer Potential of Omeprazole in Prostate Cancer Cells

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Introduction and Aim: Prostate cancer is the second most common type of cancer in men worldwide. Proton pump inhibitors used widely in gastritis disease are used as anti-cancer agents by drug repurposing. Omeprazole is a proton pump inhibitor and an FDA-approved anti-acidic drug used in acid-related diseases. The anti-cancer potential of omeprazole has been demonstrated in many cancer types. The aim of our study is to carry out in vitro experiments to shed light on the clinical use of omeprazole in prostate cancer.

Materials and Methods: 2D studies were performed. After 2D studies, 3D culture studies and scratch assays were performed to determine the effect of omeprazole on spheroid forming and migration capabilities of cancer cells, respectively. Finally, GLUT and V-ATPase assays were performed.

Results: The IC50 scores of PC-3, LnCap and CCD1072-sk cells were determined. Omeprazole inhibited significantly the numbers and size of PC-3 colonies. Surprisingly, a higher amount of glucose in the medium of the control group and acidity of the medium in the drug-treated group was higher than the control group. But in the CCD1072-sk cells group, the acidity of the medium in the control group was higher than the treated group.

Conclusion: Omeprazole doesn't only inhibit V-ATPase, but also suppresses the FASN enzyme, which plays an important role in lipid metabolism in cells. In the light of these findings, cancer cells may use the glycolytic pathway more actively in response to this, since omeprazole suppresses lipid metabolism.

Keywords: Prostate cancer, drug repositioning, proton pump inhibitor, omeprazole.

Oral Presentation – 57

Acetylsalicylic acid treatment reduces cancer promoting properties of pancreatic stellate cells

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Introduction and Aim: Pancreatic cancer is a highly aggressive type due to its unique tumor microenvironment. Active pancreatic stellate cells (PSCs) are abundant in the PaCa microenvironment and can promote cancer aggressiveness by secreting growth factors and cytokines. The daily use of acetylsalicylic acid (ASA), the active component of aspirin, has been linked to low cancer incidence in various cancers, including pancreatic cancer however, there is currently no study indicating its role on pancreatic stellate cell-mediated cancer aggressiveness. Therefore, we aimed to investigate the effect of ASA on PSCs and thereby aggressiveness of pancreatic cancer.

Materials and Methods: PSCs were evaluated for active and passive states using α-smooth muscle and Oil Red O stainings. Aspirin doses of 1.25 and 0.625 mM that were not toxic for cells selected for further experiments. PANC-1 and BxPC-3 PaCa cell lines were treated with the CM collected from non-treated (NT) PSCs and 24h ASA-treated PSCs. Changes in cell viability, migration, and invasion were evaluated using SRB assay, wound healing, matrigel invasion and colony formation assays, respectively. The difference in CM collected from PSCs after ASA pre-treatment was elucidated by ELISA and changes in released IL-6 levels were measured.

Results: The study revealed that PaCa cells exhibited increased proliferation, migration, and invasion when exposed to CM from NT PSCs, while these aggressive characteristics decreased when incubated with CM from ASA-treated PSCs.

Conclusion: ASA-treatment decreased cancer-promoting abilities of PSCs by possibly changing its secretome. Further research is needed to reveal exact mechanism of ASA on PSCs.

Keywords: pancreatic cancer, pancreatic cancer tumor microenvironment, asetylsalicylic acid.

Oral Presentation – 58

Evaluation of Circulating Tumor Cell (CTC) Specific Markers and CTC Status in Metastatic Colorectal Cancer Patients by Immunomagnetic Cell-Selection Method

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Introduction and Aim: Detection of circulating tumor cells (CTC) has great potential for assessing the risk of metastatic colorectal cancer (mCRC). However, testing for CTC is not yet part of the clinical routine due to the cumbersome methodologies and concerns about sensitivity issues. Here, we evaluated the CTC status (CTC positive/CTC negative) of metastatic CRC patients and detection rates of CTC-specific markers by immunomagnetic cell-selection method to utilize the CTC status as a clinical parameter and assess the risk of metastasis development.

Materials and Methods: Peripheral blood samples were collected from 48 mCRC patients and CTC status was determined by using AdnaTest ColonCancer technology which characterizes tumor cells based on colon-specific surface markers (CEA, EGFR and EpCAM). All samples were grouped into their CTC status [CTC-positive (presence of ≥1 CRC-specific mRNA markers) or CTC-negative] and evaluated by other clinical parameters.

Results: A total of 30 (62,5%) patients were found to be CTC-positive of which 7 patients had only EGFR-positive CTC whereas CEA positivity was observed in only one patient. However, both EGFR and CEA markers were detected in 22 of 30 CTC positive. Beta-actin expression was analyzed for each sample, and all were positive. We did not detect EPCAM positivity in any samples.

Conclusion: Our preliminary results provide knowledge to liquid biopsy investigations to consider CTC status as a clinical parameter by incorporating other clinical data for precisely assessing the risk of CRC metastasis. Future studies including larger cohorts by analyzing additional biomarkers will pave the way for the development of novel translational medicine approaches.

Keywords: metastatic colorectal cancer, circulating tumor cells, liquid biopsy, tumor markers, immunomagnetic cell selection.