ABSTRACT PRESENTER:
Gal Markel

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CURRENT SUBMISSION:
New Submission

PLEASE MARK THE RELEVANT FIELDS THAT APPLY FOR YOUR ABSTRACT:
TRANSLATIONAL RESEARCH

HEADLINE:
High throughput analyses in a cohort of melanoma patients treated with adoptive cell transfer therapy

BACKGROUND:
The clinical efficacy of PD-1 blocking antibodies is impressive, but far from fulfilling the full potential of immuno-oncology. Thus, new therapeutic targets and strategies, as well as predictive biomarkers are in great need.

MATERIALS AND METHODS:
We conducted systematic retrospective high throughput proteomic and microRNA analyses of clinical samples obtained from 40 patients treated at the Ella Lemelbaum Institute of Melanoma with adoptive transfer of tumor infiltrating lymphocytes (TIL), segregated as Responders (n=20) and Non-responders (n=20). Proteomics was performed using Super-SILAC mass spectrometry. MicroRNA profiling was performed with NanoString. Stringent statistical approach, learning algorithms and bioinformatics were implemented in order to identify significant differential signatures that can point on prominent biological processes and potential novel targets, or serve as a predictive signature. Protein expression was silenced with siRNA. Transfection of microRNA into TIL was done using BTX technology. Cytotoxicity was measured by LDH release assays. Proliferation was tested with standardized XTT.

RESULTS:
280 differentially expressed proteins were identified in the melanoma specimens of responders and non-responders. A rationalized analysis identified high aerobic tumor metabolism directly with immune sensitivity. Concurring with published data in PD-1 treated patient cohorts, proteins of the IFNg pathway were differentially expressed. We further narrowed down to a 13-protein signature that sharply discriminates between responders and non-responders. Systematic knockdown of all 13 proteins in different melanoma-autologous TIL pairs identified several novel proteins, which clearly affect the interaction between melanoma and lymphocytes. In addition, the microRNA profiling within the TIL cell product identified 2 microRNAs that were associated with failure of therapy. Transfection of these microRNAs into TIL was consistently suppressive and they probably operate by modulating the TGFb receptor and Notch signaling pathways. MicroRNA profiling in the melanoma specimens did not reveal significant data that can be translated into mechanistic insights or practical therapeutic approaches.

CONCLUSIONS:
Unbiased high throughput analyses identified a compact signature that could predict response to TIL therapy. Its value remains to be tested in larger patient cohorts treated with different immuno-oncology agents. Further, novel potential targets for therapy were identified, both in TIL and melanoma, and will be further investigated.
ABSTRACT PRESENTER:
Alberto Gabizon

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Alberto Gabizon

CURRENT SUBMISSION:
New Submission

PLEASE MARK THE RELEVANT FIELDS THAT APPLY FOR YOUR ABSTRACT:
TRANSLATIONAL RESEARCH

HEADLINE:
New insights and evolving role of pegylated liposomal doxorubicin in cancer therapy

BACKGROUND:
We herein review various pharmacological and clinical aspects of pegylated liposomal doxorubicin (PLD), the first nanomedicine to be approved for cancer therapy. There is a substantial gap between its potent antitumor activity in preclinical studies and its comparatively modest achievements in clinical studies and limited use in clinical practice.

MATERIALS AND METHODS:
PLD is a complex formulation of doxorubicin based on pharmaceutical nanotechnology with unique pharmacokinetic and pharmacodynamic properties. Its long circulation time with stable retention of the payload and its accumulation in tumors with high vascular permeability both result in important advantages over conventional chemotherapy.

RESULTS:
The ability of PLD to buffer a number of undesirable side effects of doxorubicin, including a major risk reduction in cardiac toxicity, is now well-established and confers a major added value in a number of disease conditions. PLD is approved for the treatment of ovarian cancer, breast cancer, multiple myeloma, and Kaposi sarcoma. In addition, clinically significant antitumor activity of PLD has been reported in a number of other cancer types, including lymphomas and soft tissue sarcomas. In spite of this, PLD has not replaced conventional doxorubicin in common applications such as the adjuvant and neoadjuvant treatment of breast cancer, and its use in the clinic has not become as widespread as one may have predicted.

CONCLUSIONS:
Exploiting the unique pharmacology of PLD, analyzing its selective biodistribution and homing to tumors in cancer patients with proper theranostic tools, and harnessing its complex interaction with the immune system, will lead to a more selective and rational use of PLD that may have great impact on future clinical results and may help realize its largely untapped potential.
ABSTRACT PRESENTER:
Amos Gelbard

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CURRENT SUBMISSION:
New Submission

PLEASE MARK THE RELEVANT FIELDS THAT APPLY FOR YOUR ABSTRACT::
TRANSLATIONAL RESEARCH

OTHER:
Immunotherapy

HEADLINE:
Zinc in Cancer Therapy

BACKGROUND:
Hypothesis The Immunotherapeutic theory suggests that by enhancement of the immune system's function it by itself could overcome any type of Cancer and it's symptoms. The immune system operates through the entire body, therefore igniting it could supposedly cure any Cancer regardless of it's location. Zinc Deficiency is a condition in which lack of Zinc leads to weakness of the immune system. On the other hand, high levels of Zinc are known to cause auto-immune conditions in which the immune system is enhanced to the point it attacks it's own body. Therefore, it's plausible to assume the role of Zinc as an enhancer of the immune system, a substance that, in compliance with the said theory, can lead to an ignited immune activity and enable the body to overcome any type of cancer

MATERIALS AND METHODS:
The 1st clinical study referenced,[2] examines cancer patients who were given oral administration of Zinc and Selenium and then were tested by multiple parameters. The 2nd study[3] tested tumor burden and size in cancerous mice treated with zinc supplementation. The next research[4] examined plasma levels of Zinc, among other parameters, in young patients suffering from leukemia, through different stages of the disease. The following researches[5,6] examined accumulated public dietary data and another study examined zinc levels in malignant tissue cells in-situ[7].

RESULTS:

CONCLUSIONS:
These findings brought together show definite connection between Cancer and Zinc. It brings evidence of zinc supplementation possibly being an effective treatment to different forms of Cancer. It proves Zinc levels in blood and tissue to be significantly decreased during the disease and shows proof that higher dietary zinc intake reduces cancer risk. It also shows proof that zinc supplementation can reduce tumor size and tumor burden, at least in mice. I strongly recommend further examination of these findings in order to find out if Zinc supplementation can infact enable reduction of tumor size, increase survival rates and serve as an effective treatment for any type of Cancer
ABSTRACT PRESENTER:
Irit Ben-Aharon

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CURRENT SUBMISSION:
New Submission

PLEASE MARK THE RELEVANT FIELDS THAT APPLY FOR YOUR ABSTRACT:
TRANSLATIONAL RESEARCH

HEADLINE:
miR-125a-induced cellular switch to elicit a response to anti-HER2 targeted therapy in gastric cancer cells.

BACKGROUND:
HER2 (ERBB2) amplification in gastric cancer ranges from 6-23%, accordingly Trastuzumab has been incorporated into the treatment arsenal of HER2-enriched gastric cancer. We had previously demonstrated the miR-125a-3p induces overexpression of HER2 in basal-like breast cancer cells and sensitizes them to anti-HER2 therapy (AACR-NCI-EORTC 2015). We aimed to study the effect of miR-125a-3p as a potential modulator of the ERBB2/HER2 pathway in HER2-negative gastric adenocarcinoma

MATERIALS AND METHODS:
We generated stable KATO-III cells that overexpress miR-125a-3p and control cells that overexpress scrambled miRNA. Relative mRNA level of ERBB2 was measured by qPCR and its protein expression and localisation were examined by western blot and immunofluorescence staining. Moreover, the effect of miR-125a-3p alone or combined with anti-HER2 therapies on cellular proliferation was evaluated using EdU incorporation and XTT assays

RESULTS:
miR-125a-3p-overexpressing KATO cells showed a significant increase in the expression level of ERBB2 mRNA and protein as well as a stronger immunofluorescence staining of ERBB2 on cell membrane compared with control cells. Trastuzumab reduced cell growth and proliferation of miR-125a-3p-overexpressing KATO cells. Furthermore, this antiproliferative effect was enhanced following pre-treatment of the miR-125a-3p-overexpressing KATO cells with lapatinib, a dual ErbB1 and ErbB2 receptor tyrosine kinase inhibitor, prior to trastuzumab administration.

CONCLUSIONS:
Our results indicate that miR-125a-3p is capable of inducing a shift in the expression and function of ERBB2 pathway that may convert the fate of gastric cancer cells to effectively dispose them to anti-HER2 therapies. In an era of personalized medicine, our study proposes a means to enlarge the patient population that may benefit from anti-HER2 therapies.
ABSTRACT PRESENTER:
Aron Popovtzer

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CURRENT SUBMISSION:
New Submission

PLEASE MARK THE RELEVANT FIELDS THAT APPLY FOR YOUR ABSTRACT::
TRANSLATIONAL RESEARCH, RADIOTHERAPY, Head and neck

HEADLINE:
The impact of molecular profiling guided targeted gold nanoparticles on radiosensitivity of metastatic salivary gland Adenoid Cystic Carcinoma

BACKGROUND:
Molecular Profiling has an established role in selection of treatment for metastatic disease, however its role in improving radiosensitivity and improving functional imaging has not been evaluated. The main goal of this study was to evaluate the role of molecular profiling as a method to target gold nanoparticles (GNP) in order to enhance radiosensitivity. A second goal was to evaluate the role of molecular profiling as a tool to improve our functional imaging abilities. We have chosen a metastatic Adenoid Cystic Carcinoma (ACC) tumor as a model.

MATERIALS AND METHODS:
16 nude mice were implanted with human parotid ACC found to have an Anaplastic Lymphoma Kinase (ALK) receptor mutation. The mice were treated with radiation, Crizotinib, GNP and radiation, and GNP conjugated to Crizotinib with radiation, and followed for four weeks.

RESULTS:
We demonstrated that ALK targeted GNP enhanced the radiation effect and had a significant impact on tumor growth (P

CONCLUSIONS:
Molecular profiling for targeting GNP can serve as a method to enhance radiosensitivity and improve imaging in salivary gland ACC
ABSTRACT PRESENTER:

hovav nechushtan

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CURRENT SUBMISSION:

New Submission

PLEASE MARK THE RELEVANT FIELDS THAT APPLY FOR YOUR ABSTRACT::

TRANSLATIONAL RESEARCH,LUNGS

HEADLINE:

Serine 207 phosphorylated LysRS predicts disease-free survival in non-small-cell lung carcinoma

BACKGROUND:

We have previously described a signal transduction pathway in which serine 207 phosphorylated lysyl-tRNA synthetase (P-s207 LysRS) is released from the cytoplasmic multi-tRNA synthetase complex (MSC) into the nucleus, where it activates the transcription factor MITF in stimulated cultured mast cells and cardiomyocytes. Here, we investigated the activation of this pathway in human lung cancer and its prognostic value in patients after primary surgery of their cancer.

MATERIALS AND METHODS:

To assess the roles of this pathway in cancer cells, we produced an antibody specific for P-s207 LysRS. This antibody was used in our in vitro work and retrospective study consisting of 242 tissue micro-array (TMA) samples derived from non-small-cell lung cancer (NSCLC) patients.

RESULTS:

EGF stimulation of lung adenocarcinoma cells caused serine 207 phosphorylation and nuclear localization of LysRS in-vitro. Positive nuclear staining for P-s207 LysRS was noted in 44.3% of the patients with epidermal growth factor receptor (EGFR) mutation as compared to 29.4% in wild type EGFR patients (p = 0.013, confidence interval [CI] 95%, n = 242). The mean disease free survival (DFS) of EGFR-mutated patients with nuclear serine 207 phosphorylation was 66.9 months compared to 48 months for those without phosphorylated s207 LysRS (p = 0.005, confidence interval [CI] 95%, n=140). Conversely, in wild type EGFR patients the DFS was 45.7 months compared to 52.6 months, respectively (p = 0.033, confidence interval [CI] 95%, n=102). Patients with mutated EGFR and negative lymph node metastases had better DFS with positive nuclear staining for P-s207 LysRS 67.6 months, compared with patient with negative nuclear P-s207 LysRS 52.4 months (p = 0.046, confidence interval [CI] 95%, p = 104). In addition, we noted that patients with absent lymph node metastases were positive for nuclear P-s207 LysRS (p = 0.021, confidence interval [CI] 95% ).

CONCLUSIONS:

For the first time, we demonstrate the relationship between the EGFR signaling pathway and LysRS in cancer. The data presented strongly suggests functional and prognostic significance in non-small-cell lung cancer.
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CURRENT SUBMISSION:
New Submission

PLEASE MARK THE RELEVANT FIELDS THAT APPLY FOR YOUR ABSTRACT::
TRANSLATIONAL RESEARCH,Breast,GN

HEADLINE:
Skeletal Muscle Measures as Predictors of Toxicity, Hospitalization, and Survival in Patients with Metastatic Breast Cancer Receiving Taxane Based Chemotherapy

BACKGROUND:
Severe skeletal muscle (SM) loss (sarcopenia), is associated with poor cancer outcomes including reduced survival and increased toxicity. This study investigates SM measures in metastatic breast cancer (MBC) patients receiving first line taxane-based chemotherapy and evaluates associations with treatment toxicity and other outcomes.

MATERIALS AND METHODS:
Using computerized tomography (CT) images taken for the evaluation of disease burden, skeletal muscle area (SMA) and density (SMD) were measured at the 3rd lumbar vertebrae. Sarcopenia was defined as Skeletal Muscle Index (SMI=SMA / height^2)

RESULTS:
MBC patients (N=40), median age 55 (rang 34-80), 58% sarcopenic, median SMG 1296 AU (SD 522). Grade 3-4 toxicity was found in 57% of sarcopenic vs 18% of non-sarcopenic patients (p=0.02). Toxicity-related hospitalizations were also higher in sarcopenic patients (39% vs 0%, p=0.005) as were any adverse events -- defined as any grade 3-4 toxicities, hospitalizations, dose reductions, or dose delay -- (74% vs 35%, p=0.02). Low SMG was associated with grade 3-4 toxicity (p=0.04), hospitalization (p=0.01) and time to treatment failure (for progression or toxicity) (p=0.03). Low SMG had a borderline significant association with any adverse event (p=0.06) and overall survival (p=0.07).

CONCLUSIONS:
SM measures are associated with toxicity outcomes and survival in MBC patients receiving first line taxane-based chemotherapy. Further studies are needed to explore how routinely obtained CT scans can be used to individualize dosing and improve treatment planning.
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CURRENT SUBMISSION:
New Submission

PLEASE MARK THE RELEVANT FIELDS THAT APPLY FOR YOUR ABSTRACT:
TRANSLATIONAL RESEARCH, Breast

OTHER:
Oncogenetic

HEADLINE:
A TP53 missense mutation in breast cancer patients of Arab descent

BACKGROUND:
Hereditary cancer comprises more than 10% of all breast cancer cases. Identification of germinal mutations enables the initiation of a preventive program that can include early detection or preventive treatment and may also have a major impact on cancer therapy. Several recurrent mutations were identified in the BRCA1/2 genes in Jewish populations which enable fast and cheap diagnosis and allow an estimation of hereditary cancer syndrome prevalence in this population. However, in other ethnic groups in Israel, no recurrent mutations were identified to date. Our group established panel sequencing of 22 hereditary cancer related genes to identify recurrent, founder, and new mutations in the heterogeneous and diverse populations in Israel.

MATERIALS AND METHODS:
We evaluated germline mutations using panel sequencing of 22 hereditary cancer related genes in four breast cancer patients of Arab descent diagnosed with cancer before the age of 50 years. We further tested 101 Arab cancer patients for TP53 c.541C>T using a RT-PCR approach.

RESULTS:
Utilizing panel sequencing of 22 hereditary cancer we identified the previously described TP53 mutation, c.541C>T, R181C (rs587782596), in two women from unrelated Arab families. The two probands were diagnosed with breast cancer at a young age (27 and 34 years) and had significant family history spanning a wide range of tumors (breast cancer, papillary thyroid cancer, glioblastoma multiform, colon cancer and leukemia), suggesting a recurrent mutation in this population. We further tested 101 Arab cancer patients for TP53 c.541C>T using a RT-PCR approach and identified four additional carriers, two with breast cancer, one with glioblastoma and one with lung cancer.

CONCLUSIONS:
We suggest TP53 c.541C>T testing for Arab women with a breast cancer at a young age, Arab patients with multiple malignancies, or with suggestive family history.
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CURRENT SUBMISSION:
New Submission

PLEASE MARK THE RELEVANT FIELDS THAT APPLY FOR YOUR ABSTRACT::
TRANSLATIONAL RESEARCH,Breast

HEADLINE:
Body Composition as a Predictor of Toxicity in Patients Receiving Anthracycline Based Adjuvant Chemotherapy for Breast Cancer

BACKGROUND:
Poor body composition is associated with inferior cancer outcomes including increased toxicity and reduced survival; however, in early breast cancer there is a paucity of evidence regarding body composition’s impact on outcomes. This study investigates associations between body composition measures and treatment toxicity in early breast cancer (BC) patients receiving adjuvant anthracyclines-taxane based chemotherapy.

MATERIALS AND METHODS:
Pretreatment computerized tomography (CT) images were evaluated for skeletal muscle area (SMA), density (SMD), and fat tissue at the 3rd lumbar vertebrae. Skeletal muscle index (SMI) (SMA/height^2) and skeletal muscle gauge (SMG=SMI x SMD) were also calculated. Relative risks (RR) are reported for associations between body composition measures and toxicity outcomes, after adjustment for age and body surface area (BSA).

RESULTS:
Body composition metrics were calculated for 151 patients with Stage I-III BC (median age 49, range 23 to 75). Fifty patients (33%) developed grade 3 or 4 toxicity, which was significantly higher in those with low SMI (relative risk (RR)=1.29, p=0.002), low SMG (RR=1.09, p=0.01), and low LBM (RR=1.48, p=.002), after adjustment for age and BSA. ROC analysis showed the SMG measure was the best predictor of grade 3 and 4 toxicity. Dividing SMG into tertiles showed toxicity rates of 46%, and 22% for lowest versus highest tertile, respectively (p=0.005). After adjusting for age and BSA, low SMG (CONCLUSIONS:
Poor body composition metrics are significantly associated with adjuvant chemotherapy toxicity in early BC. Further studies are needed to investigate how these metrics can be used to explore more precise dosing to reduce treatment related toxicity while maintaining efficacy.