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Proceedings of the American Association for Cancer Research

AACR ANNUAL MEETING **2019**

MARCH 29-APRIL 3, 2019 • Georgia World Congress Center • Atlanta, GA

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STATEMENT OF EDUCATIONAL NEED, TARGET AUDIENCE, AND LEARNING OBJECTIVES

The fight against cancer is rapidly progressing with the accelerating pace of discoveries in the basic, translational, and clinical sciences. This is due in large part to the advent of new technologies, such as advanced live imaging techniques and liquid biopsies, and our increased understanding of the importance of harnessing the power of the immune system to develop new immunotherapies. However, understanding and combating the processes of cancer initiation, progression, and response to treatment require a multidisciplinary approach. The AACR Annual Meeting brings together cancer biologists, clinical oncologists, and population scientists with engineers, computational biologists, and physical scientists to develop quantitative approaches and ask new questions to develop better strategies for curing cancer. By bridging the gap between what physicians understand about cancer biology and the clinical applications, this meeting aids basic researchers, physicians, and clinician-scientists in obtaining, synthesizing, and integrating the most current molecular-based tests to aid in the diagnosis, treatment, and prevention of cancer. Further, facilitating the interface between physicians and scientists increases the contributions of laboratory research to drug development as well as patient care, transforms the design and conduct of clinical research protocols, and creates an avenue for the rapid translation of laboratory research findings from "bench-to-bedside" for the benefit of improving patient outcomes. This meeting also acts as a forum to discuss cancer health disparities and help ensure that all patients benefit from emerging breakthroughs in research and cancer treatment.

Despite the tremendous progress in the field, cancer continues to be a global public health challenge, accounting for one in every six deaths that occur around the world. In the United States (U.S.) alone, it is predicted that 609,640 people will die from some form of cancer in 2018, making it the second most common cause of death after heart disease. One of the challenges we face is that cancer comprises more than 200 different diseases. For many of the most commonly diagnosed cancers in the U.S.—including lung, prostate, ovarian, urinary bladder, and colorectal cancer—incidence has been declining for more than a decade. However, incidence of other forms of cancer—including endometrial, liver, thyroid, skin, childhood cancer, and leukemia—has been on the rise. Incidence, diagnosis, access to treatment, and survival rates are also impacted by the cancer health disparities that exist in certain segments of the U.S. population, with older and underprivileged populations often witnessing higher incidences of cancer and mortality.

This conference will bring together over 23,000 investigators from the basic, translational, and clinical disciplines and provide them with a venue to discuss their recent advances, test new hypotheses, and establish new collaborations. To provide the most advanced technologies and treatments, it is critical to bridge the gap between physicians who are answering fundamental questions about cancer biology and clinicians who are applying the latest diagnostic and treatment advances to patient care. As the incidence of cancer continues to increase, the fields of cancer prevention and early interception offer unprecedented opportunities to decrease the worldwide burden of cancer.

After participating in this CME activity, physicians should be able to:

1. Assess the technological advances and tools, such as liquid biopsies, being used to accelerate progress in cancer research and improve early detection and early interception, with the ultimate goal of extending patients' lives and improving their quality of life.
2. Articulate how advances in precision cancer medicine are leading to improved patient outcomes.
3. Incorporate the latest research findings regarding therapies and treatment options, including immunotherapy and combination therapies, in a variety of cancer types to improve patient outcomes.
4. Formulate new strategies integrating multidisciplinary scientific and clinical research efforts towards the prevention, early detection, and interception of cancer.
5. Identify factors that impact the diagnosis, treatment, and prevention of various forms of cancers in patients from diverse populations.
6. Develop collaborations amongst physicians, researchers, and clinician-scientists to advance approaches for cancer treatment and prevention.

DISCLOSURE STATEMENT

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This activity is supported by grants and will be disclosed at the activity.

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Next Annual Meeting: April 25-29, 2020 • San Diego, California

future, we intend to analyze TMB and neoepitopes using surgical specimens of these patients and determine the efficacy of this biomarker for cancers other than NSCLC.

#2231 A simple blood base test for predicting clinical benefit of cancer immunotherapy. Luhui Shen,[1] Jianfen Chen,[2] Stephen Albert Johnston,[3] David Hong,[2] Jianjun Gao,[2] Aung Naing[2]. *[1]The Biodesign Inst. at Arizona State Univ., Tempe, AZ; [2]UT MD Anderson Cancer Center, Houston, TX; [3]The Biodesign Inst. at Arizona State Univ. and Calviri, Inc., Tempe, AZ.*

Immunotherapy with immune check point inhibitors (CPI) has dramatically transformed cancer therapy. However, only ~25% cancer patients have a positive clinical response to CPI. Moreover, the cost of the treatment and the risk of severe side effects makes it necessary to develop biomarkers to predict the benefit of the treatment. It has been shown that the tumor neoantigen load correlates with a positive response to treatment. This indicates that pre-existing anti-tumor immune responses to neoantigens can be used for the CPI response prediction. We have discovered a new source of frameshift (FS) neoantigens created by errors in RNA production in tumor cells, including the insertion and deletion (INDEL) of microsatellite regions during the RNA transcription and the mis-splicing of exons. These errors can generate FS neoantigens, which are highly immunogenic and can elicit both T cell and B cell immune response in cancer patients. We have shown that, although most antibody reactivity to FS peptides (FSPs) are personal, there are common antibodies reactive in different cancer patients, even across different cancer types. The FSPs with positive reactive antibodies can offer protection in mouse tumor models as vaccines. We thus hypothesize that antibodies reactive to FSPs in cancer patients can be used for predicting the clinical benefit of cancer immunotherapy. There is a total of~ 220,000 potential FS neoantigens that can be generated by INDELs of transcription and mis-splicing of genes. These neoantigens can be represented by ~400,000 FSPs, 15-amino acids peptides. We have created arrays of by in-situ synthesis of these FSPs. We used these array to test our hypothesis with pre-treatment serum of 40 cancer patients, from 26 different cancer types in clinical trials with CPI treatments. A total of 13 patients had a clinical response to CPI treatment. Similar to ELISA, diluted serum were applied to the FSP array, and total IgG were detected by fluorescent labeled antibody. IgG reactive to each FSP was measured by the fluorescent intensity and then median normalized within each array for the analysis. As predicted, there are common IgG antibodies reactive to FSPs in the response patients. By selecting 100 to 500 most significantly different reactive FSPs between two group patients, and trained with prediction models, such as SVM, our FSP array can reach up to 96% accuracy in the prediction of clinical response with leave-one-out validation. We hypothesize that the FSPs with positive IgG reactive in response patients may be related to anti-tumor immune response, which is need to be further investigated. We also showed that the FSP array can potentially predict the patients who may have high grade immune related adverse events with the CPI treatment. Our preliminary data indicates that the FSP array is a promising technology for predicting the clinical benefit of immunotherapy. We will expand our sample size to further evaluate this technology.

#2232 The assay of thymidine kinase 1 in sera from subjects with hematological and solid tumors with AroCell TK 210 ELISA: Comparison with TK-liaison assay and its clinical implications. Jagarlamudi Kiran Kumar,[1] Staffan Eriksson,[1] Kerstin Hamberg Levedahl,[2] Martin Höglund,[2] Mojca Zupan,[3] Joško Osredkar,,[4] Diana Cviič,[4] Urska Furar[4]. *[1]AroCell AB, Uppsala, Sweden; [2]Uppsala University, Uppsala, Sweden; [3]Blood transfusion centre, Ljubljana, Slovenia; [4]Institute of clinical biochemistry, Ljubljana, Slovenia.*

Background: Thymidine Kinase 1 (TK1) is an ATP dependent enzyme involved in DNA precursor synthesis. It is released into the blood from cells undergoing un-controlled proliferation where it forms stable aggregates. Serum TK1 activity has been used as a biomarker for diagnosis and monitoring of hematological malignancies. Several commercial assays are available for measuring serum TK1 activity but they require radioactive materials or special instruments. To overcome these, AroCell has developed the TK 210 ELISA for TK1 protein measurements. In this study, we compared the performance of the TK 210 ELISA to that of the TK-Liaison assay on sera from subjects with hematological and solid tumors Experimental Procedures Sera from patients with hematologic malignancies (N=51) were collected at the University Hospital, Uppsala. Samples from solid tumors [breast cancer (n=60); subjects with benign prostate hyperplasia or prostate carcinoma (n=60)] along with blood donors (N=102) were collected at the University Medical Centre, Ljubljana. TK1 protein levels were determined with AroCell TK 210 ELISA and TK1 activity levels by the TK-Liaison assay. Results In blood donors, the TK1 protein levels were in the range of 0.1 to 0.35 μg/L with a median value of 0.2. Men had a higher median value TK1 protein levels compared to women (0.21 vs 0.19) with no significant difference. Both the TK 210 ELISA and the TK-Liaison assays showed significantly higher TK1 levels in hematological and solid tumors compared to blood donors ($P<0.0001$). ROC curve analysis demonstrated that across all malignancies, at 96% specificity, TK 210 ELISA (cut-off value of 0.34 μg/L) gave a higher sensitivity of 0.43 compared to TK-Liaison assay (cut-off value of 10 U/L) of 0.36. The performance of the assays differed depending on the type of malignancy, TK 210 ELISA and TK-Liaison had a similar sensitivity (0.65) for hematological malignancies. However, in the case of solid tumors, TK 210 ELISA showed a higher sensitivity (0.35) compared to TK-Liaison (0.26) at a specificity of 0.96. A regression analysis of the TK 210 ELISA (y) and TK-Liaison (x) assays across all three groups gave an equation of $y = 0.15 + 0.017x$ ($rs = 0.80$, $n = 273$). The correlation value in hematological malignancies was higher than in blood donors and solid tumors (0.95 vs. 0.67 and 0.50 respectively). Conclusions This study showed that the AroCell TK 210 ELISA has a similar sensitivity and specificity to the TK-Liaison assay for hematological malignancies. However, the AroCell TK 210 ELISA demonstrated a higher sensitivity for TK1 in sera from subjects with solid tumors and this may facilitate the application of TK1 as a biomarker for solid tumors. Furthermore, the robustness and convenience of the ELISA not only overcomes the limitations of TK-Liaison but also widens the clinical applications of TK1 in cancer management.

#2233 Correlation between mutations found in FFPE tumor tissue and paired cfDNA samples. Lauren Saunders, Antonia Hur, Brittany Niccum, Asmita Patel. *Beckman Coulter Life Sciences, Indianapolis, IN.*

Cell free DNA (cfDNA) consists of small (150 - 500 bp) DNA fragments that circulate in the blood. cfDNA levels tend to be low in healthy, non-pregnant patients, and increase in patients with cancer, pregnancy, or extensive damage to tissue. cfDNA is believe to derive mostly from apoptotic cells, and biomarkers for a variety of diseases have been found in cfDNA. As cfDNA is extracted from blood, it is a non-invasive way to detect disease; however, there is some concern that cfDNA does not contain the same biomarkers as tumor tissue. This study measures the efficacy of cfDNA as a biomarker detection medium by comparing mutations found in both FFPE tumor samples and paired cfDNA samples. This study determines whether the same biomarkers are found in each sample type, and which of those can be used as biomarkers in both and which are preferred biomarkers for only a single sample type. Trends in mutation detection with the two different sample types are discussed.

#2234 Monitoring of genetic change in circulating tumor DNA isolated from Her2 positive advanced gastric cancer patients. Woo Sun Kwon,[1] Seung-Hyun Jung,[2] Yeun-Jun Chung,[2] Joong Bae Ahn,[3] Hyun Cheol Chung,[3] Sun Young Rha[3]. *[1]Songdang Institute for Cancer Research, Yonsei University College of Medicine, Seoul, Republic of Korea; [2]Integrated Research Center for Genome Polymorphism, Precision Medicine Research Center, College of Medicine, The Catholic University of Korea, Seoul, Republic of Korea; [3]Songdang Institute for Cancer Research, Brain Korea 21 PLUS Project for Medical Science, Division of Medical Oncology, Department of Internal Medicine, Yonsei Cancer Center, Yonsei University Health System, Seoul, Republic of Korea.*

Gastric cancer is the common solid cancer and a leading cause for cancer related mortality worldwide. Despite developments and improvement in diagnosis, surgical technique, chemotherapy and radiotherapy, median survival time of advanced/metastatic gastric cancer (AGC) patients who received systemic chemotherapy is between 15-18 months. Tumor heterogeneity is associated with heterogeneous genetic profiling, which lowers diagnostic precision and consequently becomes an obstacle to determining the appropriate therapeutic strategies for individual cancer patients. Therefore, predictive biomarkers for determining potential treatment strategy are needed to improve the prognosis of patients. Personalized medicine has emerged as the future of cancer care to ensure that patients receive individualized treatment specific to their needs. In order to provide such care, molecular techniques that enable oncologists to diagnose, treat, and monitor tumors are necessary. Liquid biopsy by genotyping circulating tumor DNA (ctDNA) has provided a non-invasive and real-time liquid biopsy approach in assessing tumor genomic alterations in clinical oncology. This ctDNA have been associated with poor prognosis and clinical outcome in various cancer including lung, breast and colorectal. In this study, we evaluated utility and genetic profiling of ctDNAs in AGC. Under IRB approval, blood samples were collected in Cell-Free DNA BCT® streck tubes from 14 Her2-positive. Depending on the treatment schedule, blood can be collected 2 to 5 times per patient sequentially. The isolated ctDNAs were analyzed to genetic profiling by OncoChase (95 genes) based on AmpliSeq. And tumor tissue genotyping by CANCER MASTER and compared different sample preparation con-