3363

Prognostic Value of Immune-Related Biomarkers in Resected Non-Small Cell Lung Cancer

Rajwanth R Veluswamy[1], Stephanie Tuminello, Francesca Petralia, Wil Lieberman-Cribbin, Pei Wang and Emanuela Taioli
[1]Mount Sinai School of Medicine

OBJECTIVES/SPECIFIC AIMS: Immune cells within the tumor microenvironment (TME) play an important role in the development and progression of non-small cell lung cancer (NSCLC). However, data evaluating the impact of individual immune cell types on NSCLC outcomes is limited and often conflicting. We performed a meta-analysis of existing data and used The Cancer Genome Atlas (TCGA) to evaluate the effect of several immune cells on surgical outcomes of stage I-IIIA NSCLC. METHODS/STUDY POPULATION: PubMed was searched to identify eligible studies evaluating survival of surgically resected stage I-IIIA NSCLC patients according to immune cell infiltration. Meta-analysis was performed using a linear mixed-effects model to determine overall, disease specific and progression free survival. We then used a similar patient subset found in the TCGA to validate the meta-analysis findings. For the TCGA analysis, sample-specific scores for different immune cells were computed via xCell using level three RNAseq data. After stratifying the cohort by histologic subtype, the association between each cell type and survival was assessed via Cox Regression, while adjusting for stage, gender and smoking status. RESULTS/ANTICIPATED RESULTS: From the meta-analysis (37 articles eligible; N = 8,162 patients), high levels of CD20+ B cells (hazard ratio [HR]: 0.36, 95% confidence interval [CI]: 0.15-0.85), natural killer (NK) cells (HR: 0.64, 95% CI: 0.41-1.0), and dendritic cells (0.34, 95% CI: 0.13-0.84) were significantly associated with better overall survival (OS); T regulatory cells (HR: 1.85, 95% CI: 1.35-2.54) were associated with worst OS. High CD8+ T cell infiltrates were associated with improved disease-free survival (DFS; HR: 0.85, 95% CI 0.73-0.99), while CD68+ macrophages (HR> 2.83, 95% CI: 1.28-6.24) were associated with worst DFS. In the TCGA cohort, lung adenocarcinomas rich in CD4 T cells, CD8 T cells, B cells, and NK cells were associated with improved OS in unadjusted analysis. In adjusted analysis, only NK cells were associated with improved OS (HR: 0.82, 95% CI: 0.69-0.98). There was no significant association of any immune cell type for DFS in lung adenocarcinomas and with both OS and DFS in Squamous Cell Lung Cancers (p>0.05 for all comparisons). DISCUSSION/SIGNIFICANCE OF IMPACT: The presence of tumor infiltration by specific immune cell subsets may potentially predict survival outcomes in resected stage I-III NSCLC patients. However, the impact of immune cells may not be similar in all histologic types and after adjusting for important clinical confounders.

3251

Psoas muscle caliber as a predictor of negative outcomes in elderly trauma patients

Anna Meader, MD[1], Damien Carter, MD, Dr. David Clark and Mihaela Stefan
[1]Tufts University

OBJECTIVES/SPECIFIC AIMS: Aim 1: To evaluate whether psoas muscle size on CT imaging can be used as univariate predictor for increased risk of morbidity and mortality in trauma patients 65 years or older with rib fractures. Primary outcomes will be 30 day mortality. Secondary outcomes will include length of stay, 30 day readmission rate, need for operative/procedural intervention, ICU days, ventilator days, discharge to rehabilitation. Aim 2: An eventual goal of the project will be to use the results of the single variable psoas size study to inform the development of a predictive model for readmission rate in this population based on clinical variables present at admission. METHODS/STUDY POPULATION: This retrospective cohort study will utilize the Maine Trauma Registry to conduct a database review for all persons 65 years of age and older admitted to Maine Medical Center between January 1, 2015 and December 31, 2017 with rib fracture as diagnosed by CT imaging. Psoas caliber will be measured on admission CT. Patient outcomes will be assessed via EMR review. RESULTS/ANTICIPATED RESULTS: Anticipate finding a relationship between decreased psoas caliber and increase in 30 day mortality and post trauma complications. DISCUSSION/SIGNIFICANCE OF IMPACT: If a relationship is demonstrated between decreased psoas caliber and poor outcomes in elderly patients with rib fractures, this early indicator could be used to identify those patients at most risk, for whom targeted interventions may make the greatest difference. Knowing a measure of frailty could also help guide goals of care discussions, because it would allow clinicians to have a more detailed understanding of a patient's baseline. Those patients identified as frail could be admitted to an ICU level of care and more closely monitored and treated. Alternatively, some frail patients and their families may choose to focus more on comfort and quality of life after achieving a better understanding of a patient's frailty and risk, changing the direction of care provided. Being able to identify the higher risk patients with an objective measure would allow clinicians to provide more personalized medicine.

3427

Racial and Gender Differences in Trends, Prevalence, and Outcomes for Non-alcoholic Fatty Liver Disease Hospitalizations in the US

Adeyinka Charles Adejumo[1], Gbeminiyi Olanrewaju Samuel and Lydie Pani
[1]North Shore Medical Center

OBJECTIVES/SPECIFIC AIMS: Projected to soon become the most prevalent cause of End-Stage Liver Disease, the frequency of Non-Alcoholic Fatty Liver Disease (NAFLD) has been rising in the US community. However, studies on NAFLD among inpatients are lacking. Aims: To report the 1) prevalence and trends, 2) outcomes of NAFLD associated hospitalizations in the US. METHODS/STUDY POPULATION: NAFLD cases were identified in the National Inpatient Sample (2007-2014) with ICD-9-CM codes, and the prevalence and trends over the 8-year period were calculated among different demographic groups. After excluding secondary causes of hepatic fat accumulation from the NAFLD cohorts (n = 210,660), the impact of sex, race, and region on outcomes (mortality, discharge disposition, length of stay [LOS] and cost) of NAFLD was computed with generalized estimating equations (SAS 9.4). RESULTS/ANTICIPATED RESULTS: Admissions with NAFLD tripled from 2007-2014 at an average rate of 79/100,000 hospitalizations/year (p-value < 0.0001), with a larger rate of increase among males vs. females (83/100,000 vs. 75/100,000), Hispanics vs. Whites vs. Blacks (107/100,000 vs. 80/100,000 vs. 48/100,000), and governmental-/un-insured patients vs. privately-insured (94/100,000 vs. 74/100,000). Males had higher mortality, LOS and cost than females. Blacks had longer LOS and poorer discharge destination than Whites; while Hispanics and Asians incurred higher cost than Whites. Uninsured patients had higher mortality, longer LOS and poorer discharge disposition than the privately-insured. DISCUSSION/SIGNIFICANCE OF IMPACT: Hospitalizations with NAFLD is rapidly increasing in the US, with a disproportionately

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higher burden among certain demographic groups. Measures are required to arrest this ominous trend and to eliminate the disparities in outcome among patients hospitalized with NAFLD.

3055

Reconstruction of Patient-specific Distal Airway Regeneration Patterns in COPD

Seyed Babak Mahjour[1], Kazunori Gomi[1], Samir Rustam[1], Phurbu Dolma[1], Jamuna Krishnan[1], Olivier Elemento[1], Frank D'Ovidio[2], Timothy S. Blackwell[3], Scott Randell[4] and Renat Shaykhiev[1]
[1]Weill Cornell Medical College; [2]Columbia University Medical Center; [3]Vanderbilt University Medical Center and [4]University of North Carolina at Chapel Hill

OBJECTIVES/SPECIFIC AIMS: The objective of this study was to reconstruct patient-specific distal airway patterns at the tissue- and single-cell resolution and develop personalized distal airway models based on utilization of patient-derived DABCs and autologous region-specific stromal cells. METHODS/STUDY POPULATION: Patient-specific distal airway units, containing parental small bronchiole (<2 mm in diameter, >12th generation) and daughter airway branches, including pre-terminal/terminal bronchioles, leading to alveoli (3-7 units/lung), were dissected. Epithelial and stromal cells were isolated from these units and processed for ddSeq single-cell RNA-sequencing (n=6 samples). Autologous DABCs and stromal cells were isolated, propagated, biobanked, and used for establishment of patient-specific distal airway models (3D-organoids and air-liquid interface-based airway wall model; n=10 samples). Region-specific tissue patterns were evaluated using immunofluorescence and laser-capture microdissection (LCM; n=6 samples). RESULTS/ANTICIPATED RESULTS: Single-cell-based human distal airway transcriptome map (constructed based on the analysis of >6,500 distal airway cells obtained from 6 subjects) identified physiological and COPD-relevant distal airway differentiation patterns, including distal airway-specific secretory phenotype (DASP) characterized with high expression of secretoglobins 3A2 and 3A1, surfactant proteins SFTPB and SFTPA2, and mucin 1, unique signatures of DABCs, and stromal (fibroblasts, smooth muscle, endothelial cell subpopulations) and immune (macrophage, T cells, B cell, mast cells). Immunofluorescence analysis and LCM confirmed distribution of cell type-specific markers with differential expression patterns of DABC and DASP signatures. Patient-derived DABC-stromal co-culture models reproduced 3 regenerative patterns: 1) physiological (high DABC-clonogenic potency, establishment of polarized differentiated organoids and DASP-expressing epithelia); 2) hypo-regenerative (failure of DABCs to form clones, spheres and mechanically stable differentiated epithelial barrier); and 3) hyperplastic (generation of DABC hyperplasia accompanied in some COPD samples by mucous-cell hyperplasia mimicking in vivo remodeling patterns). DISCUSSION/SIGNIFICANCE OF IMPACT: Patient-specific maps and models of distal airway regeneration patterns have been established in this study, which can be used to identify candidate pathways that mediate disease-relevant airway remodeling and potentially utilized as pre-clinical platforms for developing personalized therapeutic approaches to suppress the progression of distal airway remodeling in chronic lung diseases, including COPD.

3207

Relation between Dopamine Transporter (DAT1) polymorphism and subjective effects of alcohol among non-dependent drinkers

Soundarya Soundararajan[1], Bethany L. Stangl, Courtney L. Vaughan, Hui Sun, Falk Lohoff, Melanie L. Schwandt and Vijay Ramchandani, Ph.D
[1]National Institutes of Health

OBJECTIVES/SPECIFIC AIMS: Dopamine transporter (DAT1) gene variation is associated with reward-related phenotypes including alcohol response. There is also evidence for a potential moderating role for mu-opioid receptor (OPRM1) gene variation on the relationship between DAT1 variation and alcohol response measures. We aimed at studying the interaction between the DAT1 VNTR and OPRM1 A118G polymorphisms on alcohol consumption and subjective responses among non-dependent drinkers. METHODS/STUDY POPULATION: We employed a progressive ratio (PR) paradigm of intravenous alcohol self-administration (IV-ASA) using the Computer-Assisted Infusion System (CAIS) to assess the motivation for alcohol seeking and consumption in a sample of nondependent drinkers. We used the Drug Effects Questionnaire (DEQ) and Biphasic Alcohol Effects Questionnaire (BAES) to assess subjective response. IV-ASA measures included average breath alcohol concentration (BrAC) and total ethanol infused. Peripheral blood samples were collected for genotyping. Ethics approval was obtained from the NIH Addictions Institutional Review Board. RESULTS/ANTICIPATED RESULTS: Fifty participants completed the PR IV-ASA session after informed consent. There were significant interactions between the DAT1 and OPRM1 genotypes in subjective effects of alcohol. Simple main effects analysis showed that DAT1 10a allele carriers that were also OPRM1 G allele carriers had significantly higher scores for several measures: "feel the drug effects" ($F(1,46)=6.573$, $P = 0.014$), "feel intoxicated" ($F(1,46)=8.613$, $P = 0.005$) and "feeling high" ($F(1,46)=10.889$, $P = 0.002$) in DEQ and higher sedation ($F(1,46)=4.575$, $P = 0.038$) in BAES. The genotypes statistically significantly predicted average breath alcohol ($F(1,61) =3.295$, $p=0.044$) and total ethanol infused ($F(1,61)=3.632$, $p=0.032$. DAT1 VNTR and OPRM1 A118G polymorphisms taken together accounted for 6.9 and 7.8% of variations in average breath alcohol and total ethanol infused respectively. DISCUSSION/SIGNIFICANCE OF IMPACT: Polymorphic variations in DAT1 and OPRM1 interact with each other in determining subjective effects of alcohol in intravenous alcohol infusion assessing motivation for alcohol seeking and consumption in nondependent drinkers. These epistatic interactions in subjective effects of alcohol are salient in the context of predicting and understanding neurobiological effects of alcohol and thereby the therapeutic responses in treating alcohol use disorders.

3376

Super Bingers: Traits and Patterns Associated with High-Intensity Drinking

James Keoni Morris[1], Julia E. Swan, Josh L. Gowin, Melanie L. Schwandt, Nancy Diazgranados and Vijay A. Ramchandani
[1]National Institutes of Health

OBJECTIVES/SPECIFIC AIMS: This study attempts to evaluate the drinking patterns and traits of individuals who partake in high intensity drinking, defined as binge drinking at 2 or more times

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