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Urine Biomarker Predictors of Incident Hospitalization in People Living with HIV

Mason Lai[1] and Michelle Estrella[1]
[1]University of California, San Francisco

OBJECTIVES/GOALS: This study aims to determine 1) which urine biomarkers of kidney health measured in the ambulatory setting predict incident hospitalization; 2) to determine whether time-updated measures of ambulatory urine biomarkers and their changes/trajectories have added value over baseline alone. METHODS/STUDY POPULATION: Participants in the Predictors of Acute Renal Injury Study (PARIS), a prospective cohort of 478 HIV+ patients followed at the Johns Hopkins HIV Clinic, had sociodemographic, clinical data, and biosamples taken until hospitalization or up to 3 years annually. Among those hospitalized, clinical data and biosamples were collected serially during hospitalization and at 3 and 12 months post-discharge. For each of the 10 biomarkers measured, we will evaluate the association of the biomarker and risk of incident hospitalization using Cox hazards regression, adjusting for sociodemographics, comorbidities, HIV history, and medications. Biomarkers will be evaluated at baseline and as time-updated and change over time. RESULTS/ANTICIPATED RESULTS: We anticipate that higher baseline levels and increasing levels of urine albumin, Î±1M, Î²2M, NGAL, IL-18, KIM-1, MCP-1, YKL-40 will be independently associated with increased risk of incident hospitalization whereas higher and increasing levels of uromodulin and EGF will be associated with lower risk of incident hospitalization. These biomarkers collectively capture the following dimensions of kidney health: endothelial injury, tubular injury and function, inflammation, and fibrosis. We anticipate increased risk of incident hospitalization in HIV+ persons in the highest tertile of baseline, time-updated, and change over time biomarkers, relative to those within the lowest tertile. DISCUSSION/SIGNIFICANCE: This study will improve our understanding of the evolution of biomarkers of kidney health from the ambulatory to the hospitalized setting and will quantify the clinical implications of subclinical kidney damage among people living with HIV, a high-risk patient population with unique kidney pathophysiology.

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Longitudinal immune profiling reveals unique myeloid and T cell phenotypes associated with spontaneous immunoediting in a novel prostate tumor model

Casey Ager[1], Aleksandar Obradovic[1], Juan M. Arriaga[1], Matthew G. Chaimowitz[1], Cory Abate-Shen[1], Andrea Califano[1] and Charles G. Drake[1]
[1]Columbia University

OBJECTIVES/GOALS: Few preclinical models exist to study how tumors transition from prolonged stable disease ('equilibrium') to progressive disease ('escape'). We characterized a new murine tumor model the exhibits such behavior, and sought to identify and validate the role of unique tumor-infiltrating immune cell subsets in this process. METHODS/STUDY POPULATION: We evaluated growth of NPK-C1 (originally LM7304; received from Dr. Cory Abate-Shen at Columbia University), a cell line developed from spontaneous prostate cancer lung metastases in NPK mice (Nkx3.1CreERT2/+Ptenflox/floxKrasLSL-G12D/+R26R-LSL-YFP/+), in immune competent (C57BL/6) and immune deficient mice (J/Nu). We determined the role of CD4 and CD8 T cells in regulating the 'equilibrium to escape' growth dynamics of NPK-C1 via in vivo cell depletions at key inflection points of tumor growth. To deeply profile the immune contexture of NPK-C1 at these inflection points, we developed a 28-color immunophenotyping panel for use on a Cytek Aurora spectral flow cytometer. We performed dimensionality reduction and clustering analyses on these data using tSNE and FlowSOM algorithms within FlowJo (v10.6). RESULTS/ANTICIPATED RESULTS: We found that activated CD4 effector T cells are enriched in regressing NPK-C1 tumors, highlighting a role for CD4 T cells in antitumor immunity. CD8 T cells are also important for NPK-C1 control; specifically central memory-like cytotoxic CD8 T cells. Depletion of either CD4 or CD8 T cells during the equilibrium phase of NPK-C1 growth confirmed the role of these cells in antagonizing NPK-C1 escape. Tregs as a whole were counterintuitively enriched in regressing tumors, however high dimensional analysis reveals their significant phenotypic diversity, with a number of Treg subpopulations enriched in progressing tumors. In the myeloid compartment, we found that iNOS+ DC-like cells are enriched in regressing tumors, while CD103+ DCs are associated with late stage tumor progression. DISCUSSION/SIGNIFICANCE: In total, these analyses of the NPK-C1 model provide novel insights into the roles of lymphoid and myeloid populations throughout key phases of tumor/immune co-evolution, and highlight a role for multi-dimensional flow cytometry-based analyses to more deeply understand immune cell dynamics in the tumor microenvironment.

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A Machine Learning-based Pharmacogenomic Association Study of Major Adverse Cardiovascular Events (MACEs) in Caribbean Hispanic Patients on Clopidogrel.

Luis A. Rosario Arroyo[1], Luis Rosario-Arroyo[2], Krystal S RomÃ¡n-RodrÃguez[3], Carola F GonzÃ¡lez-LebrÃ³n[4], Ednalise Santiago[5], Mariangeli MonerÃ³-Paredes[6], Roberto A. Feliu-Maldonado[5,7], Abiel Roche-Lima[5,7] and Jorge Duconge[5,8]
[1]Universidad Ana G. Mendez, [2]Health Sciences School, Ana G. Mendez University, Puerto Rico, USA, [3]College of Natural Sciences, Department of Biology, University of Puerto Rico at RÃo Piedras Campus, Puerto Rico, USA, [4]College of Natural Sciences, University of Puerto Rico at Humacao Campus, Puerto Rico, USA, [5]Research Centers in Minority Institutions (RCMI) Program, Center for Collaborative Research in Health Disparities (CCRHD), Academic Affairs Deanship, University of Puerto Rico, Medical Sciences Campus, Puerto Rico, USA, [6]Biomedical Sciences Graduate Program, Pharmacology department, School of Medicine, University of Puerto Rico, Medical Sciences Campus, Puerto Rico, USA, [7]Integrated Informatics Services core IIS-RCMI, University of Puerto Rico, Medical Science Campus, Puerto Rico, USA and [8]Pharmaceutical Sciences department, School of Pharmacy, University of Puerto Rico, Medical Sciences Campus, Puerto Rico, USA

OBJECTIVES/GOALS: To summarize baseline characteristics and risk factors for major adverse cardiovascular events (MACEs) and develop a prediction model by testing the association between genetic variants and MACEs in Caribbean Hispanic patients on clopidogrel using machine-learning (ML) techniques. METHODS/STUDY POPULATION: This is a secondary analysis of available clinical and genomic data from an existing database of 600 Caribbean Hispanic cardiovascular (CV) patients on clopidogrel. MACEs is defined as the composite of all-cause death, myocardial

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