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### Discovery of Novel African American Genetic Risk Factors for Breast Cancer by Analyzing Whole Genome Sequencing Data of the Alabama Hereditary Cancer Cohort

Troy LoBue<sup>1</sup>, Betsy Stallworth<sup>1</sup>, Sheniqua Glover<sup>1</sup>, Isaac Mcneely<sup>1</sup>, Nancy Merner<sup>2</sup>

<sup>1</sup>Auburn University, <sup>2</sup>College of Veterinary Medicine, Pathobiology department

**OBJECTIVES/GOALS:** My research aims to discover African American breast cancer genetic risk factors. Interested in genetic predisposition, I search for inherited variants that could explain why African American women are disparately diagnosed at younger ages and with aggressive subtypes compared to other ethnicities. **METHODS/STUDY POPULATION:** Our study cohort, the Alabama Hereditary Cancer Cohort (AHCC), consists of African Americans that have had a breast cancer diagnosis indicative of hereditary breast cancer. Whole genome sequencing is conducted for AHCC breast cancer cases. Hypothesizing that African American-specific protein-truncating variants explain inherited risk, our control cohort consists of whole exome sequencing data of (~2500) African Americans from the Type 2 Diabetes Exome Sequencing Project on dbGAP. Single variant and gene-based association tests are being conducted to identify risk variants/genes. Prime editing is conducted to introduce risk variants into cancer cell lines for functional analyses. **RESULTS/ANTICIPATED RESULTS:** Preliminary studies, involving 60 breast cancer cases, have already revealed multiple African American-specific genetic variants in the nuclear and mitochondrial genome that are statistically linked to breast cancer risk. We are in the process of increasing our breast cancer sample size, aiming for significantly higher confidence. Prime editing for selected novel variants has begun in breast cancer cell lines. Functional assays will then be carried out to observe differences in cell proliferation, cell migration, and spheroid formation in the genetically edited compared to unedited cell lines. **DISCUSSION/SIGNIFICANCE:** African Americans are underrepresented in breast cancer research. This study reduces research participation gaps and identifies genetic risk variants, leading to better risk assessments and screening methods. Such discoveries can also lead to new therapeutic targets, reducing breast cancer deaths.

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### Epidemiology of Infectious Keratitis at University of Rochester Medical Center

Caroline Maretz, Rachel Wozniak

University of Rochester Medical Center

**OBJECTIVES/GOALS:** Infectious keratitis is a potentially sight-threatening disease. Its epidemiology has been considered on various national and regional levels, which demonstrates unique patterns in patient risk factors, causative organisms, antimicrobial resistance and clinical outcomes. This study will examine the patterns specific to the Rochester, NY area. **METHODS/STUDY POPULATION:** This project will be a ten-year retrospective study, examining all patients who were diagnosed with infectious keratitis at the University of Rochester Medical Center between 2011 and 2021. The study population is selected from a compiled list of those patients with an ICD diagnosis code including 'keratitis' in the eRecord that falls within

our chosen date range. Participants were excluded if the patient's physician documented that the keratitis is most likely not infectious in etiology. If eligible for the study, there is documentation of patient demographics, clinical risk factors, clinical course, culture data from corneal scraping and antimicrobial resistance patterns, if available. Once data is collected, it will be analyzed and compared to pre-existing regional and national data. **RESULTS/ANTICIPATED RESULTS:** Between 2011 and 2021, there were 1652 patients with ICD diagnoses of keratitis at the University of Rochester Medical Center. Of these patients, we anticipate approximately 1,200 to meet our inclusion criteria. Some of the major risk factors for developing infectious keratitis in this population include contact lens use, immunocompromised state (elderly, diseased or iatrogenic) and corneal trauma. Clinical complications include progression to endophthalmitis, need for interventional surgery, or failure to improve on clinical exam after 2 weeks of antimicrobials. Causative organisms are most often bacterial. Certain organisms are associated with specific risk factors while other organisms predict greater risk of complications. We also anticipate patterns of antimicrobial resistance to emerge. **DISCUSSION/SIGNIFICANCE:** This study will provide insights into the risk factors and clinical course of infectious keratitis according to causative organisms in the Rochester, NY area. This can help us mitigate risk factors and help prognosticate for patients, once diagnosed. Also, patterns of antimicrobial resistance can inform empiric antimicrobial recommendations.

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### Flavored tobacco sales restrictions and youth e-cigarette use by tobacco retailer density

Melanie Dove, Davis Kevin Gee, Davis Elisa Tong

University of California

**OBJECTIVES/GOALS:** Flavored tobacco sales restrictions (FTSR) may reduce youth tobacco use, but may not be as effective in areas with greater tobacco retailer density (TRD), which is associated with greater tobacco access and more common in low-income areas. We examined the association between FTSRs and e-cigarette use for youth in high and low TRD cities. **METHODS/STUDY POPULATION:** We analyzed data from the California Healthy Kids Survey using a difference-in-differences (DID) strategy. We compared pre- and post-policy changes in ease of access to e-cigarettes, current use, and ever use one year after implementation among students (9th and 11th graders) attending school in a city with a FTSR (n=20,832) versus without (n=66,126). Separate analyses were conducted for students in cities with low and high TRD, with a median cutoff of 3.3 tobacco retailers per square mile. **RESULTS/ANTICIPATED RESULTS:** Students attending schools in cities with high TRD (compared with low TRD) had a higher percentage of parents with a high school education or less, and were more likely to identify as Hispanic or Non-Hispanic Asian/Pacific Islander. Among students with low TRD, FTSRs were associated with reduced ease of access to e-cigarettes (DID=0.76, 95% CI: 0.58, 0.99). However, among students with high TRD, FTSRs were associated with increased ease of access (DID: 1.25, 95% CI: 1.02, 1.56) and current use (DID=1.57, 95% CI: 1.31, 1.87). **DISCUSSION/SIGNIFICANCE:** FTSRs were associated with lower youth e-cigarette access in low, but not high TRD areas. Stronger policies or enforcement may be needed in high TRD areas.