**Racial and ethnic differences in the tumor immune microenvironment of lung adenocarcinomas**

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Lung cancer is the second most common cancer and the leading cause of cancer-related death for both men and women in the United States. There are race and ethnic differences in lung cancer risk and survival, independent of smoking history. Specifically, African Americans and Native Hawaiians are at high risk for all major histologic lung cancer cell-types, even after controlling for known risk factors. A prior study identified differences in gene expression profiles in stage and histologic subtype-matched lung tumors from African American and White patients, suggesting that underlying differences in lung tumor biology contribute to the observed race and ethnic disparities in risk and survival (PMID: 29196495). To date, there are no studies that have examined race and ethnic differences in tumor biology across a large multiethnic population. To build on these findings, we conducted genome-wide methylation profiling (Infinium MethylationEPICv1, Illumina) for 279 lung adenocarcinoma FFPE tumor tissue from diverse race and ethnic backgrounds collected by the University of Hawaii Cancer Center and University of Southern California SEER tumor repositories (37 African Americans, 55 Japanese Americans, 23 Latino American, 38 Native Hawaiians/Pacific Islanders, 75 Non-Hispanic Whites, 21 Filipino Americans, and 30 other Asian Americans (primarily Chinese and Koreans). These samples were examined for differences in the tumor immune microenvironment using the *in silico* tumor cell fraction deconvolution approach (MethylCIBERSORT; PMID: 30389940). Our preliminary results indicated that when compared to Non-Hispanic Whites (referent group), we observed differences in the DNA methylation-based estimates of immune cell composition of the non-White groups, adjusting for sex and age (**Figure 1**). We found that Filipino Americans, Japanese Americans, Latinos and the Other Asian American group, but not Native Hawaiians and African Americans, had significantly lower levels of Treg cells (p=0.01). We also found that Filipino Americans and the Other Asian American group had higher levels of endothelial cells (p=0.04). In conclusion, our study found differences in the tumor immune microenvironment for lung adenocarcinomas across diverse race and ethnic populations. Future directions include evaluating these profiles in relation to lung cancer-related survival.



**Figure 1.** Differences in the extent of immune cell infiltration by race and ethnicity. Plotting the difference (95% confidence interval (CI)) from Non-Hispanic White (W) referent category based on model adjusting for age and sex; p-value is for the overall likelihood ratio test for race/ethnicity.