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Predicted Nicotine Biomarkers and Translational Research in Multiethnic Populations

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Background: Smoking remains the largest modifiable risk factor for morbidity and mortality, and tobacco related health disparities occur in multiple populations with other social and health disparities. Researchers have identified social, behavioral and genetic contributions to measures of smoking behavior and to biomarkers of nicotine metabolism and consumption. Multiethnic populations present opportunities for tobacco related genomic translational research.

Methods: We developed prediction models of urinary nicotine biomarkers from genome-wide genotypes in cigarette smokers using machine learning. We validated these models in external datasets, and evaluated concurrent and predictive validity in treatment seeking smokers.

Results: Internal correlations for the urinary nicotine metabolite ensemble were robust (r = 0.76, 0.82 and 0.67 for African, Asian and European ancestry smokers). Correlations from external validation with a variety of nicotine metabolite ratios (urine and plasma/saliva) were 0.52, 0.61 and 0.46 for African, Asian and European ancestry participants. In analysis of N=456 treatment seeking smokers (mean age 50 years, 42% female, 7.4% African American, 9.4% Multiracial, 6.5% Other Office of Management and Budget race), predicted urinary nicotine metabolite ratio predicted prospective abstinence (OR=0.57, $p<0.04$). We designed two covariate models to characterize demographic contributions; Office of Management and Budget African American race, and African genomic ancestry proportions were significantly associated with prospective abstinence.

Conclusion: The predicted urinary nicotine metabolite ratio is associated with prospective abstinence, concordant with biochemical measures and genetic models of the plasma ratio. Progress in improving smoking outcomes will benefit from analyses of diverse populations to characterize contributors to tobacco related health disparities.