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The Dual Utility of Cg05575921 Methylation in Lung Cancer Screening Decision Making: The Value of Racial and Gender Bias Free Precision Epigenetics Approaches in Guiding Low Dose Computerized Tomography (LDCT) Use and Smoking Cessation.

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DNA methylation at cg05575921 is generally accepted biomarker for smoking whose AUC for detecting smoking is 0.98 and whose reversion can be used to guide smoking cessation therapy. However, whether cg05575921 methylation can be used to guide other clinical decision making is unclear. One potential application is LDCT screening of high-risk smokers for lung cancer. LDCT screening can save lives. However, only a small fraction of those who are screened will benefit, but all will be subjected to radiation and potential harms from unnecessary biopsies. Previously, clinicians used the PLCOM2012 risk formula, but its inclusion of gender, race and SES based variables makes it not only inaccurate but ethically unacceptable. As a result, the United States Preventive Services Health Task Force (USPSTF) has called for new methods to predict lung cancer risk. In that hope, we examined cg05575921 methylation in DNA specimens from the National Lung Cancer Screening Trial (NLST) using methylation sensitive dPCR. We found that cg05575921 methylation significantly predicted risk for lung cancer, particularly among former smokers, and that a formula that uses just pack-year consumption and cg0557921 methylation predicts need for LDCT better than pack year consumption alone. We conclude that Precision Epigenetics approaches using cg05575921 methylation can not only be used to guide smoking cessation but can also be used to guide LDCT decision making. We further suggest that the teaching moment provided by Lung Cancer screening could be an opportunity to use Precision Epigenetically guided contingency management treatment of smoking and smoking associated addictions.