Prediction of Electronic Nicotine Delivery Systems Use in COPDGene Using Multi-omics Biomarkers

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Prediction of Electronic Nicotine Delivery Systems Use in COPDGene Using Multi-omics Biomarkers

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Introduction: Biomarkers may be useful for understanding the toxic effects of vaping. Herein, we identified blood transcriptomic and proteomic biomarkers of vaping, related them to prospective health outcomes, and investigated their ability to accurately distinguish vapers from smokers.

Methods: We grouped 3,892 COPDGene study participants as vapers, current smokers, former smokers, or dual users. We tested for associations with 21,471 blood RNA transcripts and 4,979 plasma proteins. We related the significant biomarkers to 6.5 years of incident health events. To assess the discriminative performance of multi-omics for vaping, we constructed linear discriminant analysis models with cross-validation for RNA and proteins considered separately and in combination. We evaluated the model performance at the optimal cutoff on the receiver-operating characteristic curve using the Youden index (YI).

Results: We identified 2 transcriptomic and 148 proteomic associations to vaping, and 25 transcriptomic and 323 proteomic associations to dual use (FDR 10%). Oncostatin M (vapers), a
cytokine signaling protein, was associated with increased respiratory mortality. *NPHPI* (dual users), a gene involved in cilia integrity, was associated with increased respiratory exacerbation and cancer mortality. The combined RNA and protein predictive model, that respectively incorporated a mean of 79 and 298 biomarkers, showed an excellent discriminative performance for dual users *versus* former smokers (*Y_I* = 0.84±0.01) and a modest discrimination for vapers *versus* former smokers (*Y_I* = 0.50±0.05). Top predictors included genes related to immunity and tumor suppression and proteins linked to interleukin signaling and vasculogenesis.

**Conclusion:** A blood-based multi-marker panel may help predict vaping and its associated long-term health outcomes.

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