Vaping-Associated Variation in Microrna Expression in Circulating Extracellular Vesicles

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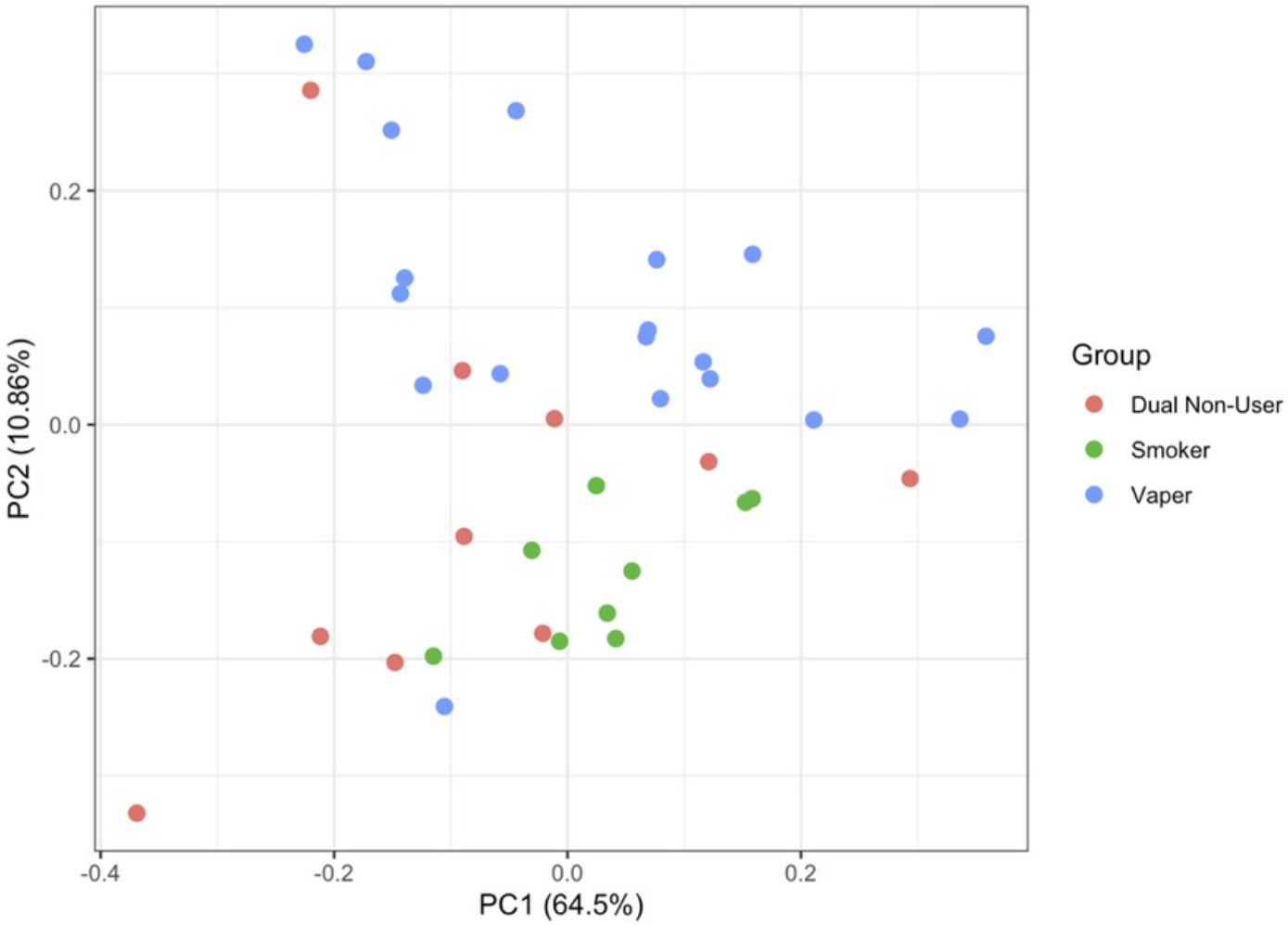
Rationale. The health effects of e-cigarette use (vaping) are poorly understood, and biomarkers of potential toxicities are needed. MicroRNAs (miRNAs) are short, noncoding RNA molecules involved in posttranscriptional regulation of gene expression; when miRNAs are packaged into circulating extracellular vesicles (EVs) and released into the bloodstream, they function as intercellular signals that can modulate systemic effects. We hypothesized that vaping would be associated with differential EV-miRNA expression compared to conventional cigarette smoking and dual non-use. Methods. We aimed to recruit 20 healthy adults ages 21-45 years who self-reported daily or intermittent vaping, plus 10 conventional cigarette smokers and 10 dual non-users who were recruited sex-, age-, and race/ethnicity-matched to vaping participants. All participants were invited to complete questionnaires regarding e-cigarette use then undergo fasting blood samples, which were processed immediately and stored at -80°C. EVs were isolated from the plasma via ultracentrifugation then suspended in lysis buffer to release EV-encapsulated RNA. The expression of a panel of 2,083 targeted miRNAs was measured with the HTG EdgeSeq miRNA Whole Transcriptome Assay. Linear regression models were used to identify genes that were differentially expressed between the exposure groups with limma in R; we applied a significance threshold of FDR<5%. Results. We successfully enrolled 38 participants (9 intermittent vapers; 10 daily vapers; 9 smokers; 10 dual non-users) with an average age of 30 years; 71% were male, 47% were Hispanic/Latino, 30% were African American, 15% were non-Hispanic White, and 8% were Asian American. Principal component analysis showed global EV-miRNA expression differed in vapers compared to both smokers and dual non-users (Figure). Pairwise comparisons between exposure groups identified specific miRNAs that were differentially expressed. In particular, 3 miRNAs were downregulated in vapers compared to dual non-users; these miRNAs did not overlap with the 70 that were differentially expressed in smokers compared to dual non-users. One of these, miR-204, has previously been implicated in pulmonary artery hypertension in both human subjects and mouse models; it is involved in regulation of the Src-STAT3-NFAT pathway, which is known to play an important role in modulating smoking-related inflammation and lung injury. Conclusion. This study is the first to identify vaping-associated changes in miRNA expression. The global shift in the miRNA expression profiles of vapers indicates there are broad molecular effects from e-cigarette use, and the specific differentially expressed miRNAs present strong candidates for biomarkers of e-cigarette toxicity and future translational research.



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