Tobacco use is a complex polygenic disorder and continues to be the leading cause of preventable death worldwide.1–3 The present issue highlights seven original investigations that address some of the complexities and gaps in the state of the science with innovative methods.

Do and Maes conducted a systematic review of gene-environment (GxE) interaction investigations4 that identified 16 studies with at least one statistically-significant GxE interaction. Due to heterogeneity of phenotypes and endpoints, no meta-analyses were possible. Melroy-Greif and colleagues5 examined a panel of single nucleotide polymorphisms (SNPs) in genes for nicotinic acetylcholine receptors and interacting genes in 9141 European-ancestry (EA) and 3947 African-ancestry smokers. Although nominal (p < .05) associations were reported for nicotine dependence and cigarettes per day, none were robust to correction for multiple comparisons.

Two studies examined genetic influences on tobacco use phenotypes during childhood and adolescence. In a first of its kind investigation, Maes and colleagues6 conducted an integrated mega-analysis of longitudinal twin studies between 1983 and 2007 in over 19,000 same-sex and opposite-sex twin pairs from the United States, Europe, and Australia. The results demonstrated remarkable consistency of findings across sexes and cultures for a decay of shared environmental effects on smoking initiation with age and increased liability of additive genetic factors on tobacco use by late adolescence. Pugach and colleagues7 investigated the potential protective effects of haplotypes of five single nucleotide polymorphisms tagging the CYP2B6 rs8192729 and CYP2A6 rs834829, and CYP2A6 rs8192729 were robustly statistically significant in combined sample analyses.

Risso and colleagues8 investigated the relationship between SNPs in the TAS2R38 bitter taste receptor gene and smoking menthol cigarettes in the first study of its kind in 718 African Americans, who are more likely to smoke menthol cigarettes than other ethnic/racial groups.9 There was an allele-dose effect of the presence of the TAS2R38 “taster” PAV haplotype, such that menthol cigarette smoking was less frequent in individuals possessing two or more copies of the PAV haplotype. These results confirm those previously reported in EA smokers10 and have important public health implications.11 In addition, a polygenic risk score based on the 11 nominal SNPs identified with statistical trend in stage 1, was significantly associated with the difficult quitting phenotype in stage 2—albeit with a small effect size.

These studies present a range of innovative approaches to filling important gaps in translation but also expose the persistent challenges of limited sample sizes, particularly for non-European study populations, the need for open and “big” data13 to enable large-scale, unbiased meta-research, and the need for evidence of clinical utility in a field justified by public health and clinical endpoints.1

References


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