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How Genomics can bring us Toward Health Equity

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Applying a sophisticated meta-analytic approach, Culverhouse and colleagues evaluated the association between CHRNB3-CHRNA6 variants and four types of substance dependence (nicotine, alcohol, cannabis, cocaine) across two large samples of European Americans and African Americans (total N = 5171) (1). The significance of their contribution is in their examination of an allele that is common across African American and European American populations (rs13273442), and *specific* to nicotine dependence, a modifiable health risk behavior that has widespread public health impact.

This evaluation is timely; it comes on the heels of the 50th anniversary United States Surgeon General's Report on Smoking and Health (http://www.surgeongeneral.gov/library/reports/50-years-of-progress/exec-summary.pdf), which reported that smoking was responsible for >480,000 premature American deaths (annually), as attributable to lung cancer (87%), pulmonary disease (61%), and coronary heart disease (32%). The Culverhouse data are also important in light of existing health disparities in tobacco use and related health outcomes across racial/ethnic groups. Mirroring patterns found among adolescents (2), compared with European Americans, African American adults continue to show much lighter patterns of tobacco use, in the face of much more severe and sustained health consequences (e.g., lung cancer) (3, 4).

In addition, large-scales studies, including by members of the Culverhouse team, indicate that African Americans have some of the lowest rates of accessing, receiving, and completing smoking cessation interventions, with some of the poorest outcomes following treatment (3, 5). Some may argue that the broader layer of health disparities in morbidity and mortality for African American smokers may be driven by socio-cultural factors, including socio-economic status (6), smoking-related health information and knowledge (7),

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and health literacy (8). They also may reflect differences in health care providers' pattern of engagement with African American patients (9).

The critical question is how genetics can help reduce these disparities. Addiction genomics offers an important new avenue to identify ideal targets for more efficacious pharmacotherapy development, which will ideally translate into personalized medicine. This avenue is not only indicated within the field of basic science, which suggests that nicotinic achetylcholine receptor (*nAChR*) subunits may serve as ideal targets for treating nicotine dependence (10), but also within the behavioral literature, which has found that African American smokers are highly interesting in and willing to undergo genetic testing in order to improve treatment matching for smoking cessation (11).

In the bigger picture, this work also represents a significant step towards reducing the paucity of knowledge around genetic risk for African Americans. Historically, many genetic studies have traditionally excluded non-European Americans in an effort to avoid population stratification (12). Fortunately, recent studies, including this one, have begun to address these substantive gaps by explicitly examining both epigenetic (13) and genetic markers associated with smoking risk and treatment response within African American samples (e.g. 14, 15-16).

In terms of the current investigation, a few points merit consideration. First, despite the immense sample size and sophisticated analytic approach, African Americans still represent a minority within this investigation (32% vs. 68%). This matters, as the effects for rs13273442 were much stronger within the European American sample (e.g., nicotine in the EA COGA sample, p = 1.4e-3) as compared with the African American sample, wherein a significant relationship was only observed for one of the three groups (e.g., nicotine in the AA COGA sample only, p = 0.03). Similarly, significant relationships for the second evaluated single nucleotide polymorphism (SNP; rs 4952) were only observed within the European American sample (nicotine in the EA COGA sample, p = 0.02; nicotine in AA samples, ns). Importantly, the direction of observed effects were the same for both cultural groups, and across both evaluated SNPs. Thus, despite these minor limitations, this study still boasts impressive strengths by evaluating a polymorphism that is common across both ethnic groups, as well as an ideal site for novel pharmocotherapy development (17), suggesting its promise as a future treatment target.

Ultimately, while both pharmacotherapy and behavioral treatments have shown some promise with African American smokers in controlled research settings (18), Culverhouse and colleagues' work highlights an important next step in this journey. Genomic information, in concert with behavioral interventions that are attentive to the cultural needs of this community (19), may offer a route to improve access and engagement in smoking cessation for African Americans (11). Yet, the most important challenge lies ahead – overcoming the barrier between treatments that seem scientifically compelling, and those that are truly accepted by members within this community is the critical next step in achieving health equity.

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