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Epigenetic Signatures of Adiposity in Ugandan Populations: An Epigenome-Wide Association Analysis RODAM Study

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Background: Although epigenome-wide association studies (EWAS) have linked DNA methylation to obesity, a critical knowledge gap exists for sub-Saharan African populations, who bear a disproportionate obesity burden. Our study addresses this gap through an EWAS of adiposity metrics in Ghanaians.

Methods: The Illumina 450k DNA methylation array was used to profile DNA methylation in whole blood samples of 547 Ghanaians from the Research on Obesity and Diabetes among African Migrants (RODAM) study. Differentially methylated positions (DMPs) and differentially methylation regions (DMRs) were identified for BMI and obesity (BMI ≥ 30 kg/m2), as well as for waist circumference (WC) and abdominal obesity (WC ≥ 102 cm in men, ≥88 cm in women). All analyses were adjusted for age, sex, blood cell distribution estimates, technical covariates, recruitment site and population stratification. We also did a replication study of previously reported EWAS loci for anthropometric indices in other populations.

Results: Our analysis revealed 18 DMPs for BMI, 23 for WC, three for obesity, and one for abdominal obesity. Notably, 14 DMPs overlapped between BMI and WC, with cg00574958 (CPT1A) emerging as a key DMP associated with all outcomes, explaining 6.1% and 5.6% of variance in obesity and abdominal obesity, respectively.

Conclusions: This pioneering EWAS on adiposity in Africans revealed three epigenome-wide significant loci (CPT1A, NLRC5, and BCAT1) linked to both general and abdominal adiposity, laying groundwork for understanding DNA methylation's role in sub-Saharan African adiposity.