Admixture Mapping of Brazilians Identifies New Obesity Susceptibility Loci

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Human obesity reached epidemic proportions and it imposes a public health and economic challenge of our time. It has been estimated that >40% of the individual variability of BMI, a common measurement of obesity, is attributed to genetic components. However, the genetic basis of obesity remains mostly unexplained. Genome-Wide Association Studies have identified at least 97 loci associated with obesity that only explain ~2.7% of the BMI variability. In this context, an effective but overlooked source to identify new genetic variants associated with obesity is the admixed genomes of Brazilians (European, African and Native American parental populations) using an Admixture Mapping strategy. This approach considers the differences in the prevalence of obesity between parental populations to find genomic regions that have enhanced ancestry of the parental populations with greater prevalence of the trait. Using this approach, we are working on an Admixture Mapping of BMI in Brazilians. We analyzed data of >2.28 million SNPs of three Brazilian cohorts, being 1,309 children from Salvador, 3,736 adults from Pelotas and 1,442 elderly people in Bambui. We aim to expand the catalogue of genetic variants associated with obesity and gain a better understanding of obesity in several age groups. Besides, we also are generating a pipeline which will facilitate further studies of Admixture Mapping of other diseases in Brazilians and other admixed populations. We found a significant positive correlation of BMI with African ancestry (rho=0.032, p-value=0.048) and a negative correlation with European ancestry (rho=-0.04, p-value =0.034) in Pelotas. In Bambui cohort, we observed the opposite results of Pelotas, a negative correlation of BMI with African ancestry (rho=-0.06, p-value=0.031) and a positive correlation with European ancestry (rho=0.06, p-value=0.023). In Salvador there were no significant correlations of BMI with African or European ancestry (p-value=0.447 and 0.456, respectively). Correlation of Native American ancestry with BMI was not observed in any of the three cohorts. We identified new obesity susceptibility loci on chromosomes 10, 13, 16 and 20. We found that loci at 10q22.1-3 and 13q12.3 are associated with obesity in the children cohort of Salvador, while loci at 16q12.1 are associated with the adult obesity in Pelotas and at 20p12.1-2 with the female adult obesity in Pelotas. Our study highlights the potential of Brazilian genome to gain a better understanding of the genetic basis of diseases and it also provides a pipeline that supports future Admixture Mapping studies in trihybrid populations.