Using estimates of individual admixture to study the genetics of phenotypic traits: skin pigmentation in African Americans.

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The availability of molecular panels has been important in the practical application of most genetic mapping methods. Here we report on a panel of ancestry-informative markers (AIMs) that demonstrate high allele frequency differences between Africans and Europeans. These AIMs can be used to estimate the European and African proportional ancestry at the population sample level, subgroup level (e.g. cases and controls for a dichotomous phenotype), and individual level. Estimates at both the subgroup and individual level can be very instructive regarding the genetics of the phenotypes of interest and provide the foundation for mapping the genes underlying these traits (Admixture Mapping). Using skin pigmentation as a model phenotype, we demonstrate how such studies could proceed. We typed 21 AIMs, of which 4 were candidate genes for skin pigmentation differences between Africans and Europeans, in a sample of African American individuals from Washington, DC. The allele frequency difference between Africans and Europeans ranged from 36% to 99.7%. We observed a strong correlation between estimates of individual admixture and skin pigmentation (measured by the melanin index). When analyzed individually, 9 of the AIMs, including 2 candidate genes, showed significant association with skin pigmentation. The high rate of association between AIMs and an ancestry-dependent phenotype, in this case skin pigmentation, indicates that the trait is genetic, and that there is a significant degree of population structure in the sample. In order to correct for this structure, we used the estimate of individual admixture as a covariate. After making the correction, only one candidate gene, oculocutaneous albinism type 2 (OCA2), remained significant, and none of the other AIMs showed association. These results indicate that OCA2 is one of the genes contributing to the differences in pigmentation levels between African and European populations.

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