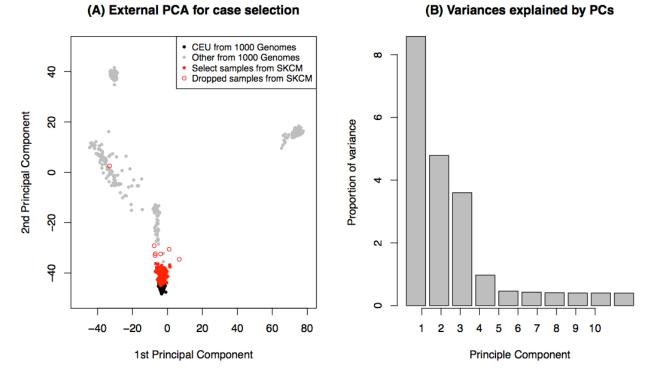
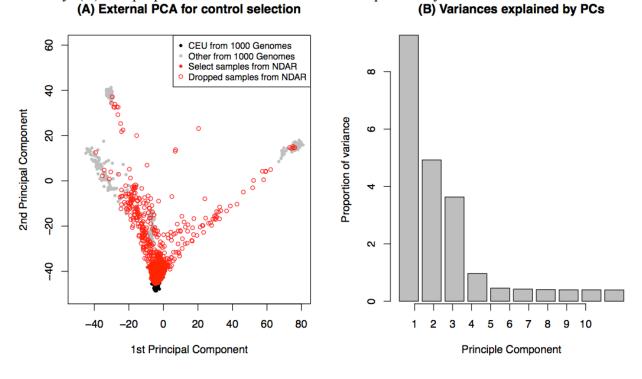
## **Supplementary Figures**

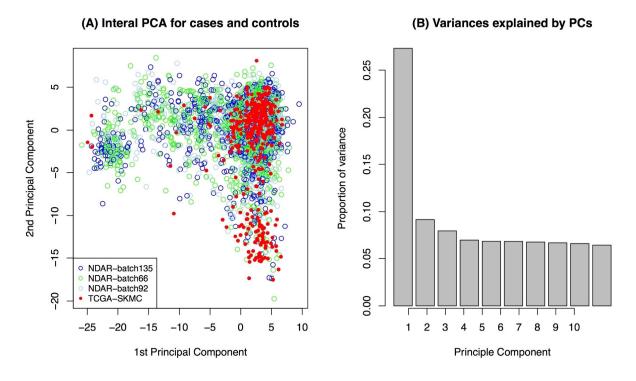
**Figure S1. Principal component analyses of TCGA melanoma cases.** We used the external PCA in XPAT to project the case individuals onto PCA space constructed using data from the 1000 Genomes Project. (A) The plot of PC1 and PC2 before and after selecting samples of European ancestry. (B) The proportion of variances that can be explained by the first 10 PCs.



**Figure S2. Principal component analyses of NDAR controls.** We used the external PCA in XPAT to project the controls individuals onto PCA space constructed using data from the 1000 Genomes Project. (A) The plot of PC1 and PC2 before and after selecting samples of European ancestry. (B) The proportion of variances that can be explained by the first 10 PCs.



**Figure S3. Internal PCA of cases and controls.** We conducted the internal PCA with selected cases and controls together. (A) The plot of PC1 and PC2 for cases and controls. (B) The proportion of variances that can be explained by the first 10 PCs.



**Figure S4.** The quantile-quantile (q-q) plot presented the expected and observed p values from VAAST2-MGIT analysis. We tested genes with at least four testable variants that could have possible conservation-controlled amino acid substitution matrix scores (CASM scores) in VAAST 2's framework. Blue dots: QQ plot of p values from gene-based association tests without using XPAT's cross platform QC criteria. Red dots: QQ plot of p values from gene-based association tests using XPAT.

