Abstract: It is frequently of interest to determine whether the effect of an independent variable, such as a SNP, on a dependent variable, such as some phenotype of interest, proceeds through mediating variables, such as gene expression. This analysis is difficult when the number of potential mediators is larger than the sample size. We propose new inference procedures for the indirect effect in the presence of high-dimensional mediators for linear mediation models. We also show that in certain cases, our procedure can lead to more powerful association tests, compared to methods that do not leverage data from mediators. We illustrate our approach in an integrative analysis of gene expression and genotype data from a pharmacogenomic study of drug response. We present a novel analysis of gene sets to understand the molecular mechanisms of drug response, and also identify a genome-wide significant noncoding genetic variant that cannot be detected using standard analysis methods.