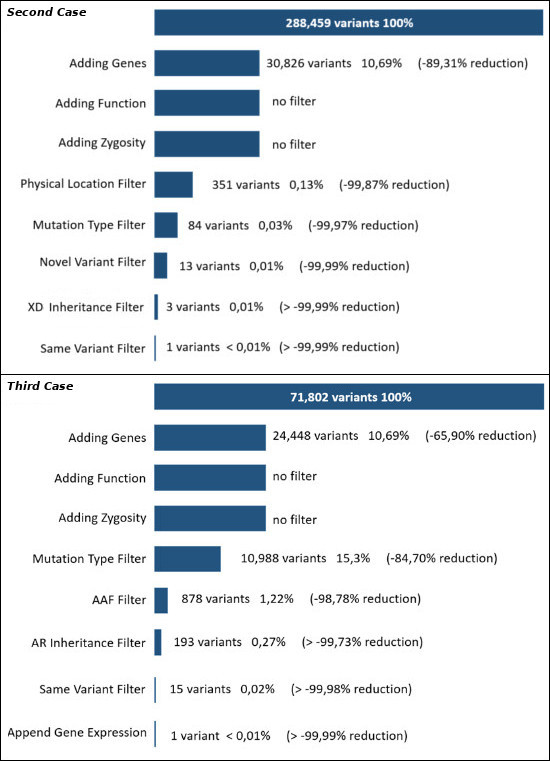
**Supplementary Data**

*Figure S1: Annotation and filtering cascade of unique variants across all case VCF input files. Both case studies annotated variants against a hg19 gene map comprised of exons, introns, UTR, splice sites, and 500bp promoter regions. Variants that did not fall within any of these sites were deemed wholly-intergenic and discarded from the analysis. (Top) Second Case study makes use of prior genetic linkage data which highlighted a locus of interest on the X chromosome, and was used in conjunction with the X-linked Dominant Inheritance Filter to reveal 1 causative missense variant. (Bottom) Third Case study looked only for rare non-synonymous coding variants by applying the Mutation Type and AAF filters in conjunction with an Autosomal Recessive Inheritance Filter, which when combined with additional organ-specific gene expression data, resulted in one disease-causing variant.*

**Pipeline Module Overview**