Quality Control Filtering Step | Number of SNPs | Number of SNPs removed | Number of SNPs remaining |
--- | --- | --- | --- |
Total number of identified variants | 278,639 | - | - |
Removed sites with > 5% missing genotyping | 278,639 | 14,242 | 264,397 |
Removal of X and Y chromosome variants | 264,397 | 6,218 | 258,179 |
Removed synonymous and intronic variants | 258,179 | 131,744 | 126,435 |
Removed sites without variation | 126,435 | 2,841 | 123,594 |
Excess heterozygosity filter | 123,594 | 211 | 123,383 |
Minor Allele Frequency ≥ 0.2 | 123,383 | 83,848 | 39,535 |
Removed variants not predicted to be damaging by PloyPhen2/SIFT | 39,535 | 26,784 | 12,751 |

**Table S1: Quality control filters used in WES Analysis.** Sex chromosomes were removed, as gender did not impact HbF response to hydroxyurea. Sites with heterozygous to homozygous ratio >0.4 were removed. Variants with MAF<2% were analyzed by burden testing.
Supplemental Figure 1: Distribution of patient HbF Values. The normal distribution of the change in HbF at MTD (A) and final HbF at MTD (b) in our study population is demonstrated.
Supplemental Figure 2: Q-Q plot of p-values from WES study of 171 sickle cell patients treated with hydroxyurea. Association between variants and ΔHbF and final HbF at MTD are shown, providing evidence of departure from null distribution.