Supplementary Figure Legends:

Supplementary Figure 1: Pairwise LD (R^2) heatmap for all SNPs reported in HapMap ±2kb of the *STAT3* gene.

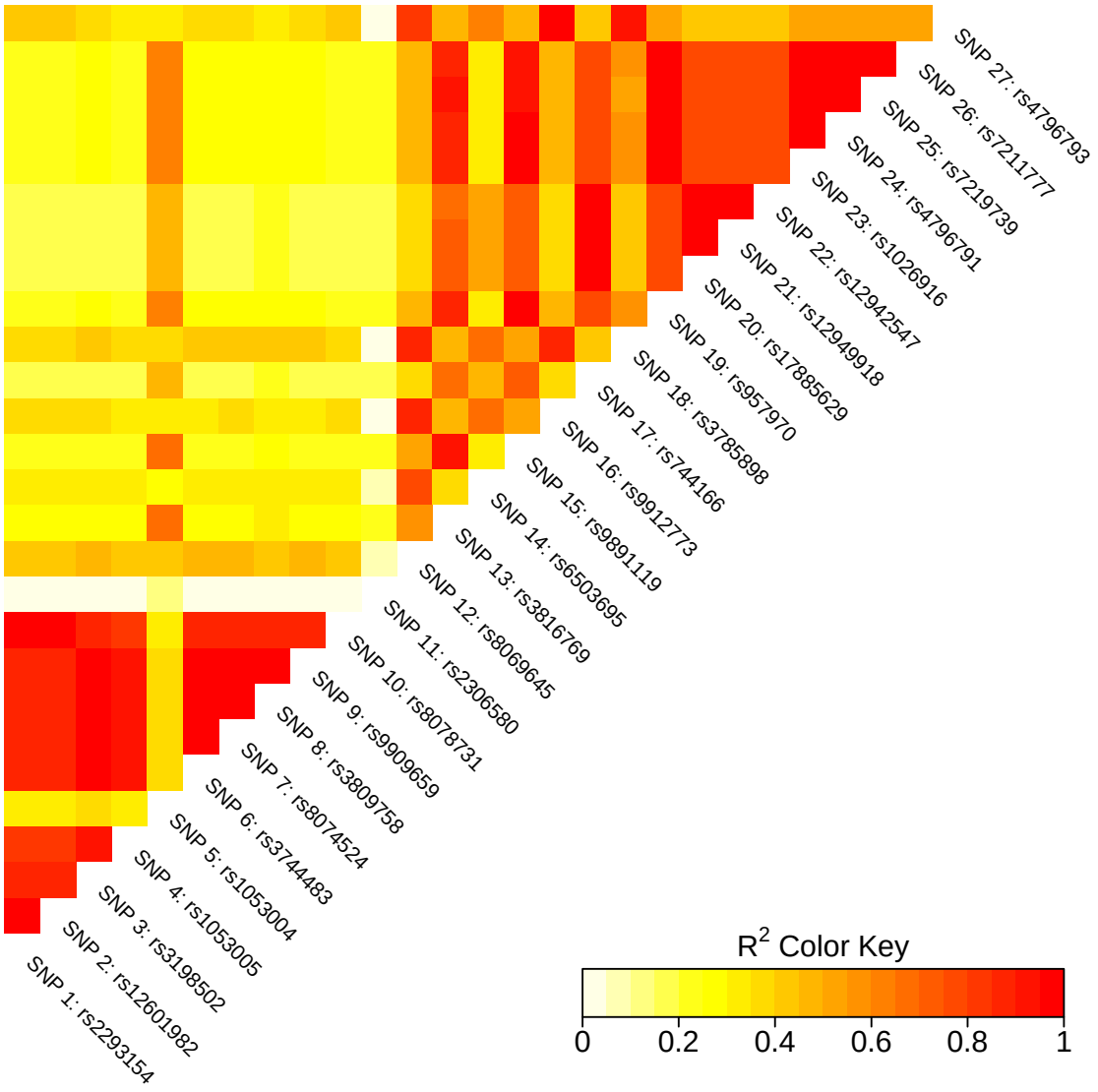
Supplementary Figure 2: Power for the W2WK (red), traditional joint (blue), and traditional main effect (green) approaches by causal SNP under the M2 model. An "x" marks the 14 SNPs that were modeled as genotyped in our simulations. The MAF of each SNP (grey line) is along the right Y-axis. Plot on the left assumes an additive model; the plot on the right assumes the underlying model is dominant, but was tested as additive. Inset plot shows the underlying model (M2): solid black line represents genotypic effect among individuals who have been exposed to the environmental insult. Dotted black line shows genotypic effect of individuals who were not exposed to the environmental insult under the M2 model. Dotted grey lines indicate alternate models that are considered elsewhere in this manuscript.

Supplementary Figure 3: Power for the W2WK (red), traditional joint (blue), and traditional main effect (green) approaches by causal SNP under the M4 model. An "x" marks the 14 SNPs that were modeled as genotyped in our simulations. The MAF of each SNP (grey line) is along the right Y-axis. Plot on the left assumes an additive model; the plot on the right assumes the underlying model is dominant, but was tested as additive. Inset plot shows the underlying model (M4): solid black line represents genotypic effect among individuals who have been exposed to the environmental insult. Dotted black line shows genotypic effect of individuals who were not exposed to the environmental insult under the M4 model. Dotted grey lines indicate alternate models that are considered elsewhere in this manuscript.

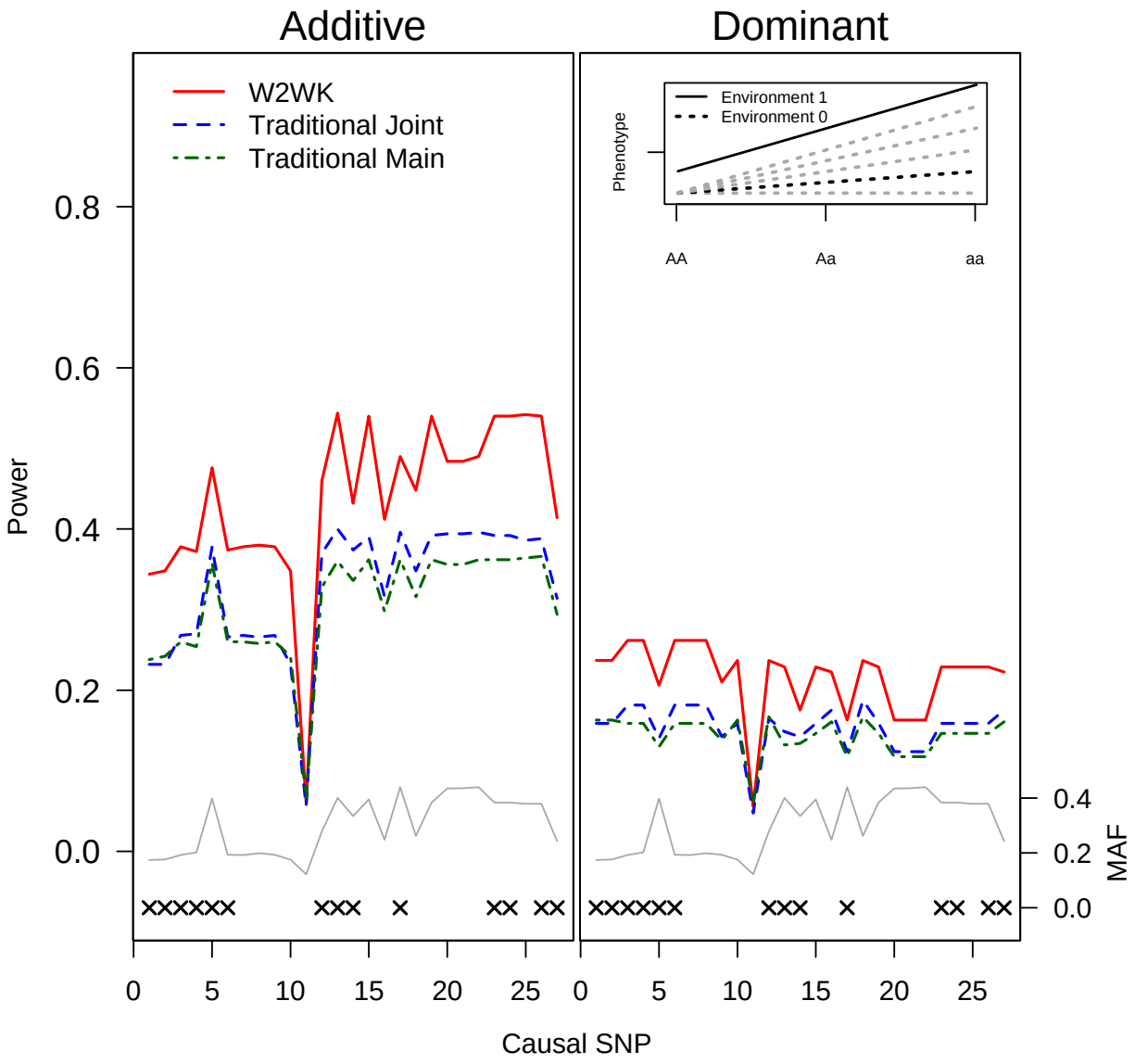
Supplementary Figure 4: Power is plotted as a function of median R^2, assuming additive effects. We define median R^2 as the median squared correlation of the causal SNP with the genotyped SNPs in our SNP set. Our W2WK is shown in red, traditional joint test is shown in blue, and the traditional main effect test is shown in green.

Supplementary Figure 5: Power for the W2WK (red), traditional joint (blue), and traditional main effect (green) approaches by causal SNP under the M1-M5 additive models. In addition, we show the power to detect an effect using an unweighted two-way interaction kernel (cyan). When MAF of the causal SNP is greater than ~0.35, an unweighted kernel approach is slightly more powerful than the weighting scheme we selected for our W2WK approach.

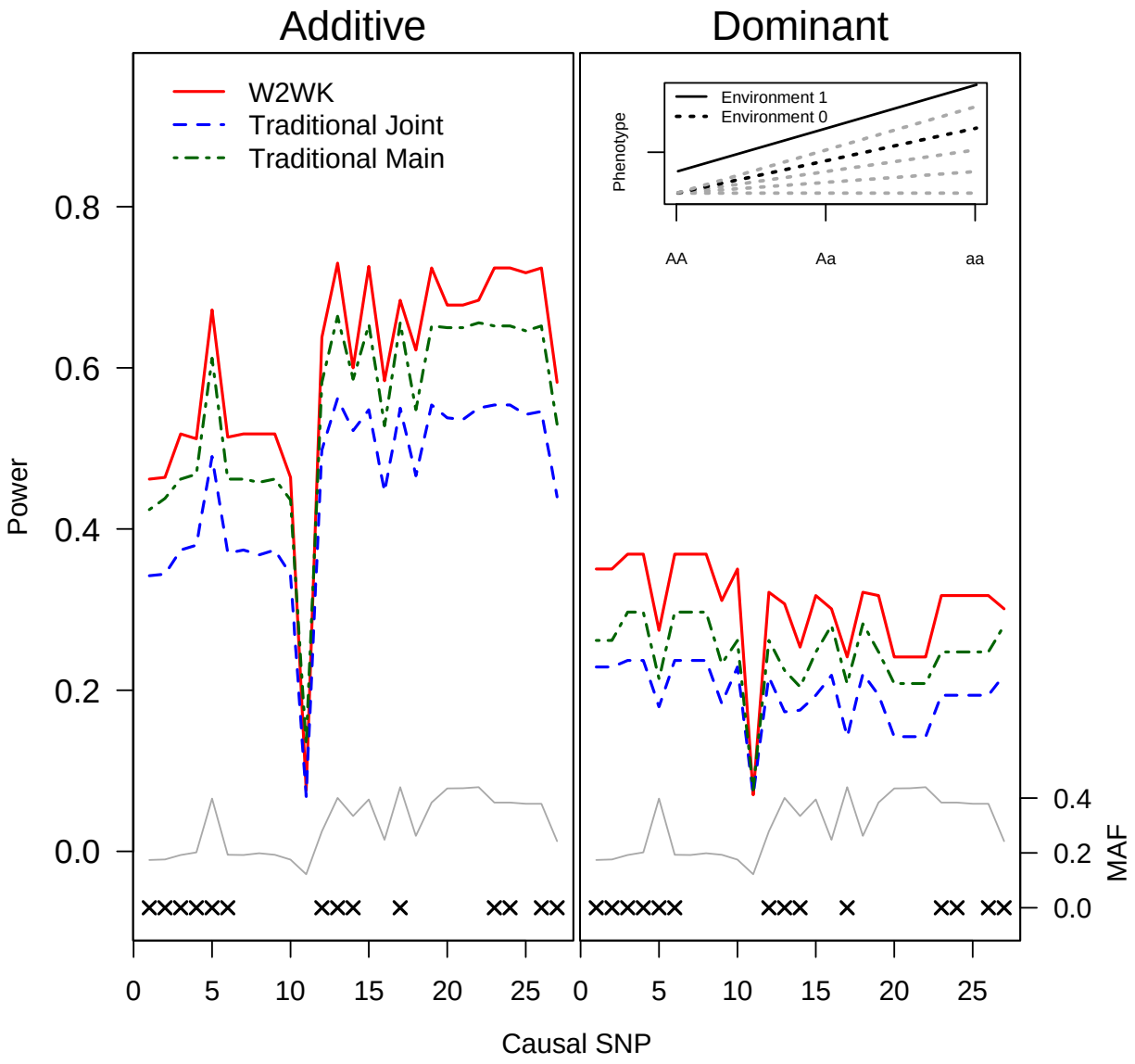
Supplementary Figure 1: Pairwise LD of *STAT3*



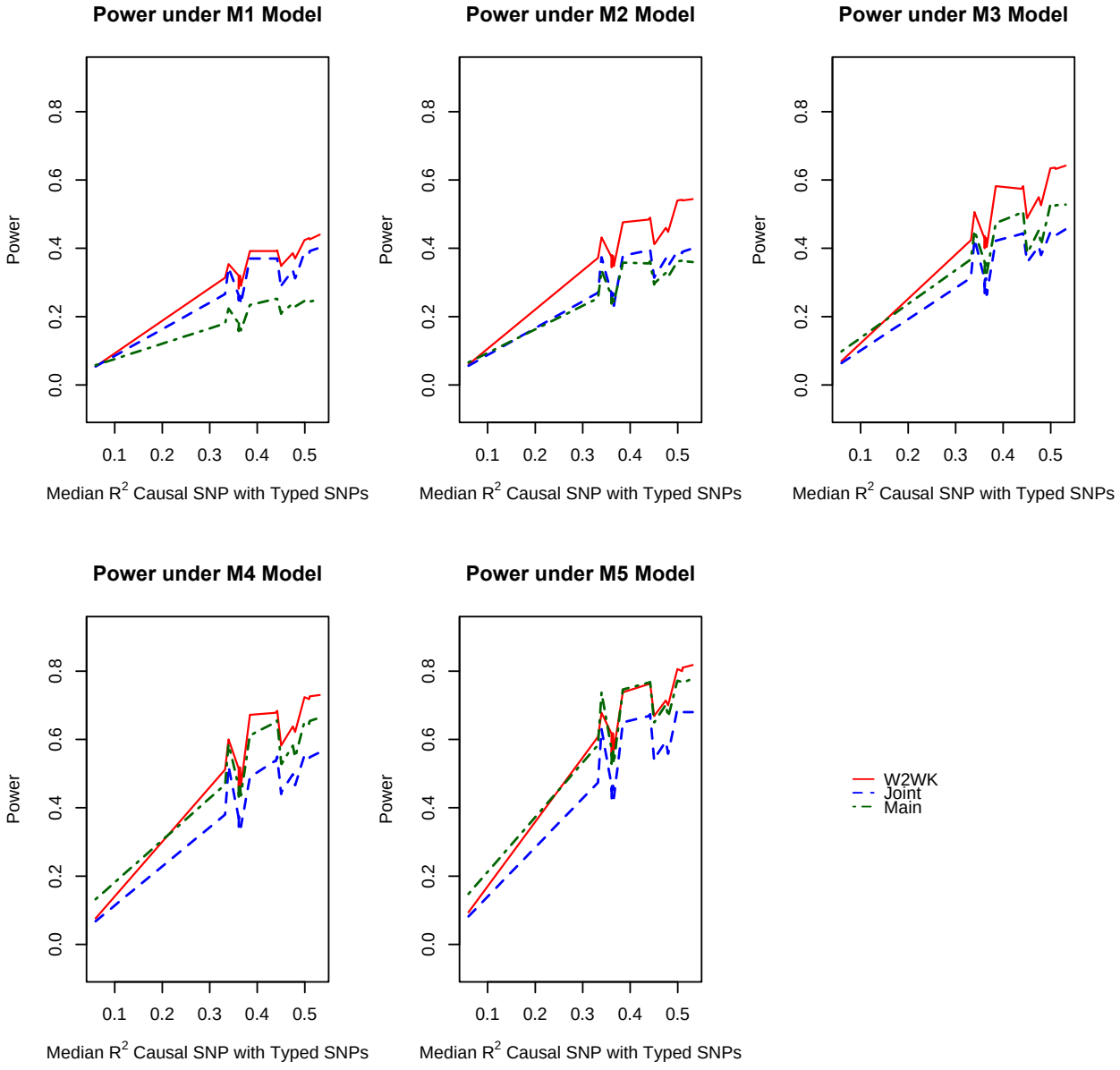
Supplementary Figure 2: Power under M2 Model



Supplementary Figure 3: Power under M4 Model



Supplementary Figure 4: Power as a Function of Median R^2



Supplementary Figure 5: Power as a function of causal SNP MAF