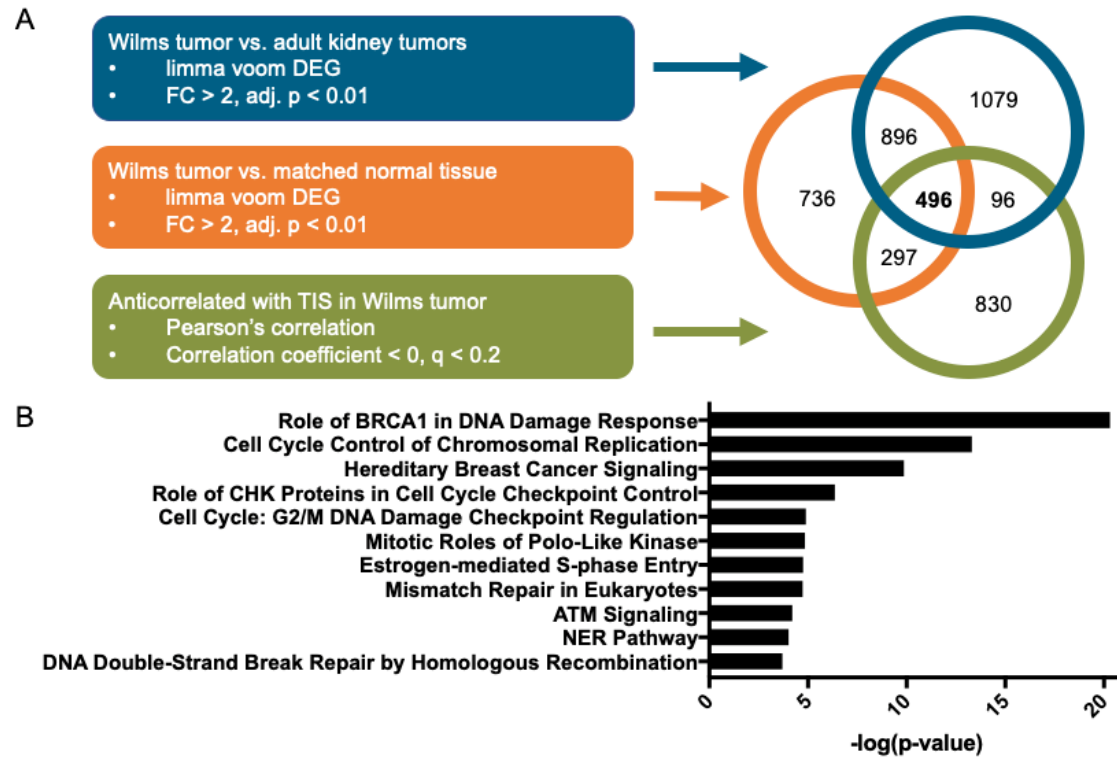
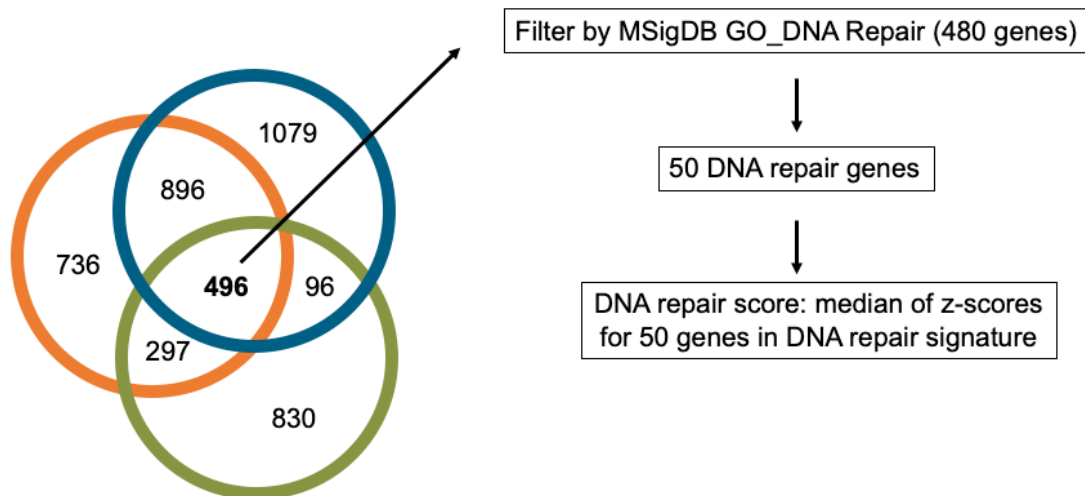


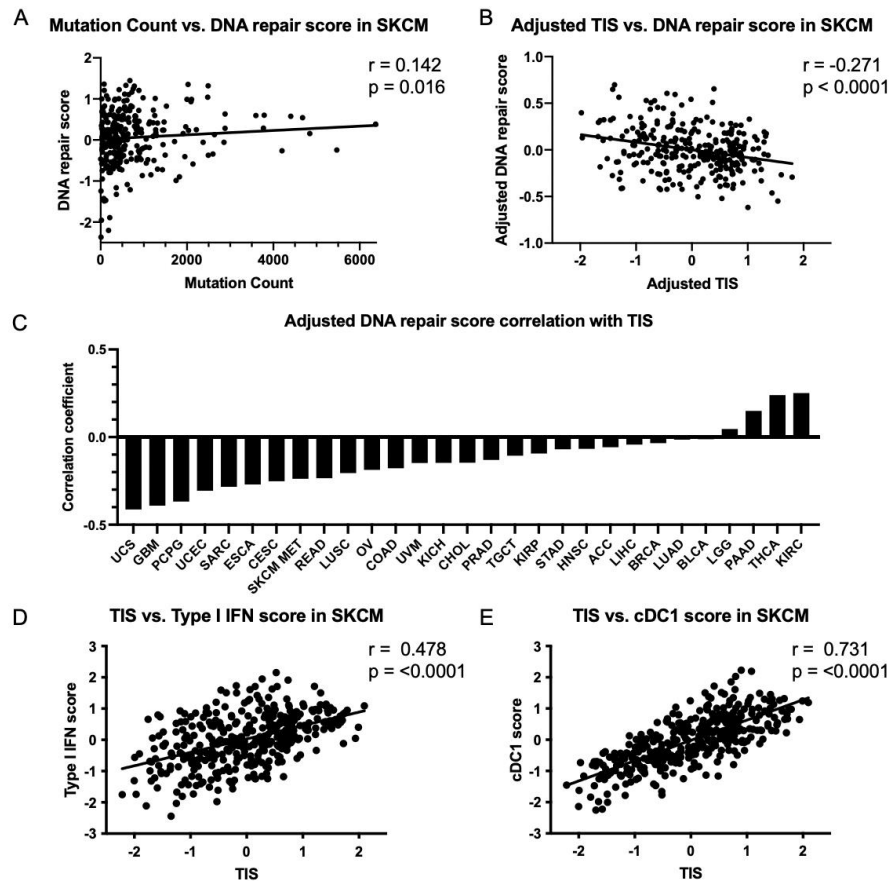
Supplementary Figures



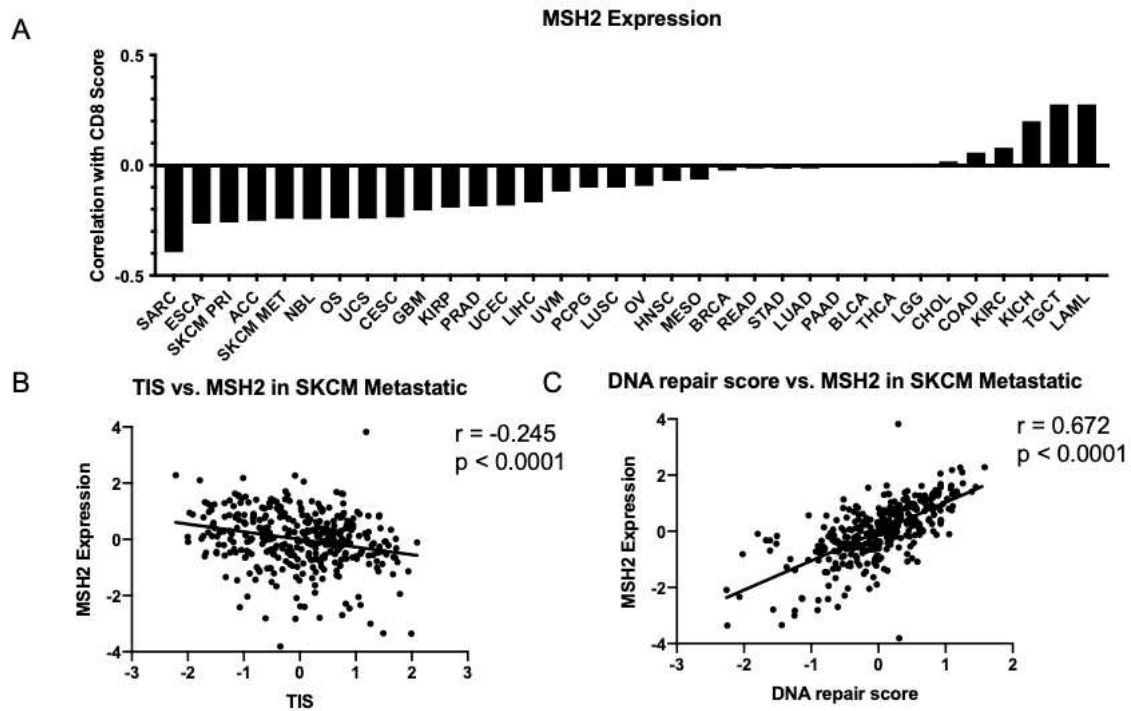
Supplementary Figure 1 | Genes upregulated in Wilms tumor and anti-correlated with TIS associate with DNA damage response and repair pathways. a Venn diagram of candidate genes identified by three independent methods. **b** Top pathways identified by Ingenuity Pathway Analysis for 496 candidate genes.



Supplementary Figure 2 | Method for developing DNA repair score. A list of relevant DNA repair genes was curated by starting with the 496 genes identified as significantly upregulated in Wilms tumor compared to adult kidney cancers, upregulated in Wilms tumor compared to matched normal tissue, and most strongly anti-correlated with TIS in Wilms tumor. This list was then filtered for DNA repair genes using the 480 genes present in the MSigDB GO DNA Repair gene signature, resulting in 50 genes that were related to DNA repair, upregulated in Wilms tumor, and anti-correlated with TIS in Wilms tumor. A z-score was calculated from the \log_2 -normalized expression of each gene in the signature, and the DNA repair score was calculated as a median of z-scores for the 50 signature genes.



Supplementary Figure 3 | TIS strongly associates with Type I IFN score and cDC1 score but not with total mutation count in melanoma, and DNA repair score correlation with TIS is not explained by TMB. a Correlation between DNA repair score and total mutation count in TCGA metastatic melanoma samples. Pearson's correlation $r=0.142$, $p=0.016$. **b** Correlation between TIS and DNA repair score in TCGA metastatic melanoma, adjusted to regress out effect of TMB. Pearson's correlation $r=-0.271$, $p<0.0001$. **c** Correlation coefficients for correlation between TIS and DNA repair score in each TCGA tumor type, adjusted to regress out effect of TMB. **d** Correlation between TIS and Type I IFN score in TCGA metastatic melanoma. Pearson's correlation $r=0.478$, $p<0.0001$. **e** Correlation between TIS and cDC1 score in TCGA metastatic melanoma. Pearson's correlation $r=0.731$, $p<0.001$.



Supplementary Figure 4 | MSH2 expression significantly anti-correlates with TIS in most TCGA tumor types, including melanoma. a Correlation coefficients for the correlation between MSH2 expression and TIS in each TCGA tumor type. **b** Correlation between TIS and MSH2 expression in TCGA metastatic melanoma samples. Pearson's correlation $r = -0.245$, $p < 0.0001$. **c** Correlation between DNA repair score and MSH2 expression in TCGA metastatic melanoma samples. Pearson's correlation $r = 0.672$, $p < 0.0001$.