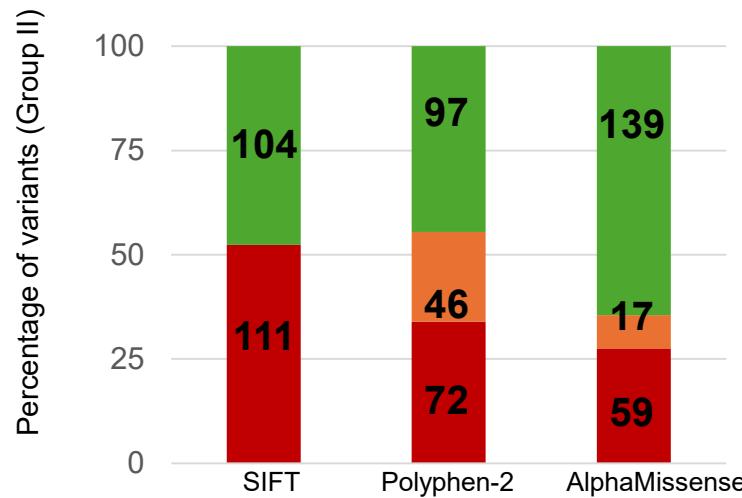
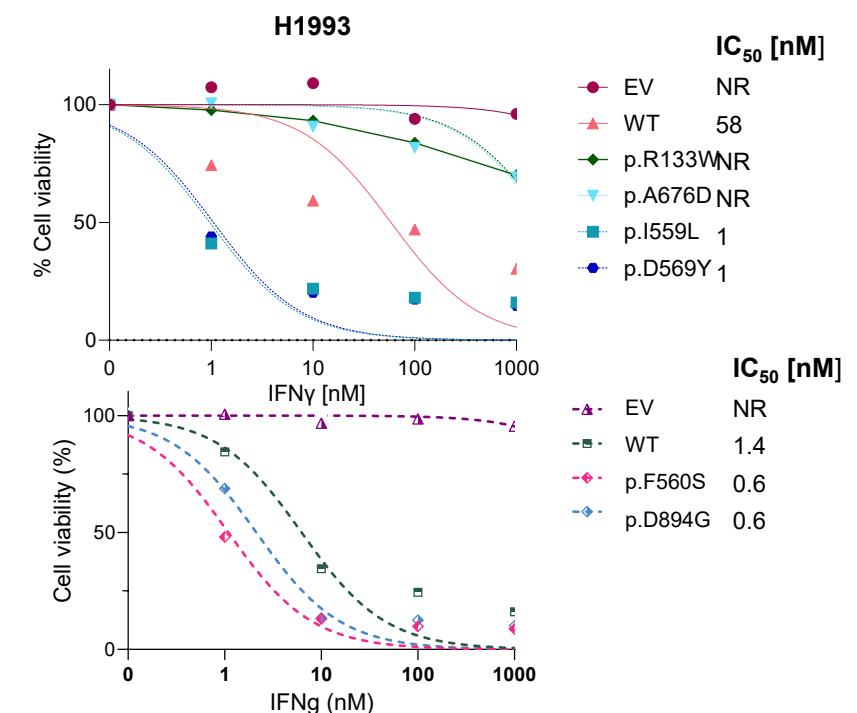
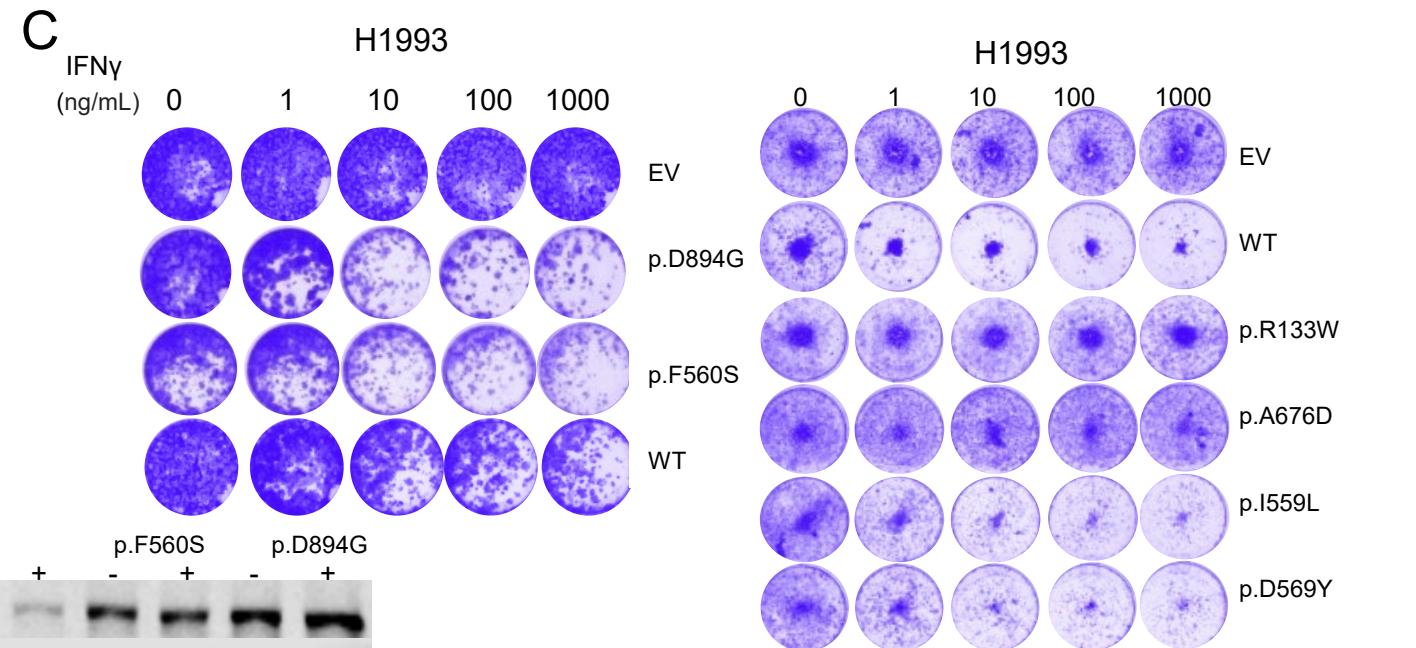
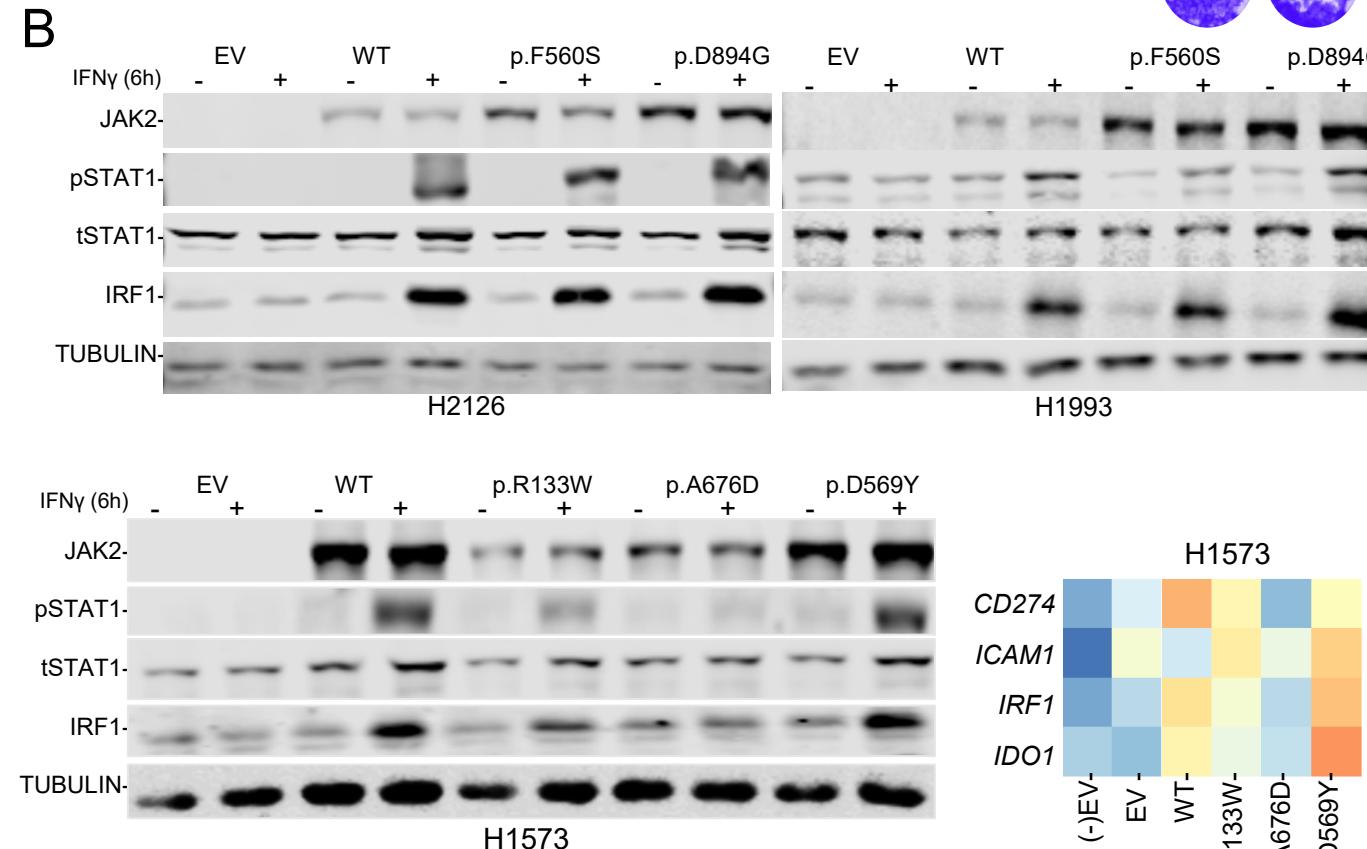
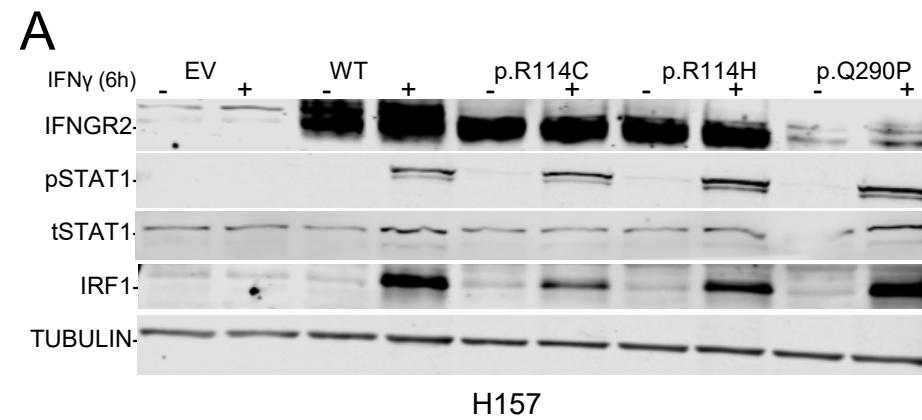


Deleterious/Probably Damaging/Pathogenic  
Possibly Damaging/Ambiguous  
Tolerated/Benign/Benign



**Supplementary Fig. 1.** Bar graphs showing the distribution of different mutational categories for each indicated algorithm. Numbers within the bars indicate the total count for each category.



## Supplementary Figure 2

**Supplementary Fig. 2.** **A**, Western blot showing protein levels in the indicated cancer cells ectopically expressing different mutant forms of IFNGR2, compared with wild-type (WT) and empty vector (EV) controls, following treatment with IFN $\gamma$  (30 nM). **B**, Western blot showing protein levels in the indicated cancer cells ectopically expressing different variants of JAK2, compared with wild-type and empty vector (EV) controls, following treatment with IFN $\gamma$  (30 nM). Panel on the right, heatmap showing changes in mRNA levels, based on quantitative RT-PCR (relative to *Actin*), of selected IFN $\gamma$  target genes in the indicated cancer cell lines ectopically expressing the specified mutant proteins. **C**, Upper panel, representative clonogenic assays for the indicated cells infected with EV and WT or the indicated mutants and treated for 10 days with IFN $\gamma$  at the indicated concentrations or untreated. Lower panel, viability of indicated cell lines and conditions, as in **B**. Lines, number of viable cells relative to the untreated cells. NR, not reached. IC<sub>50</sub>, half maximal inhibitory concentration.