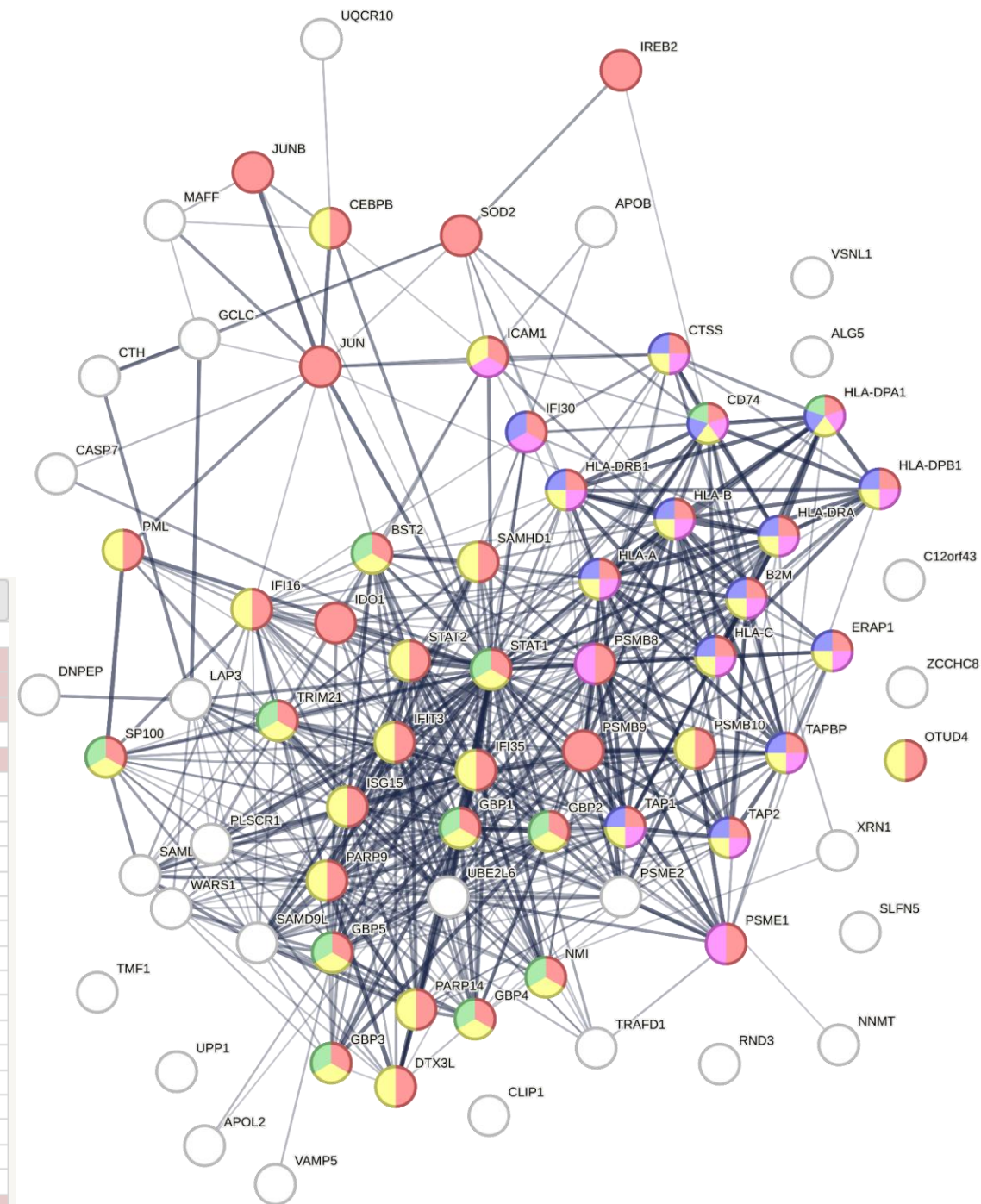


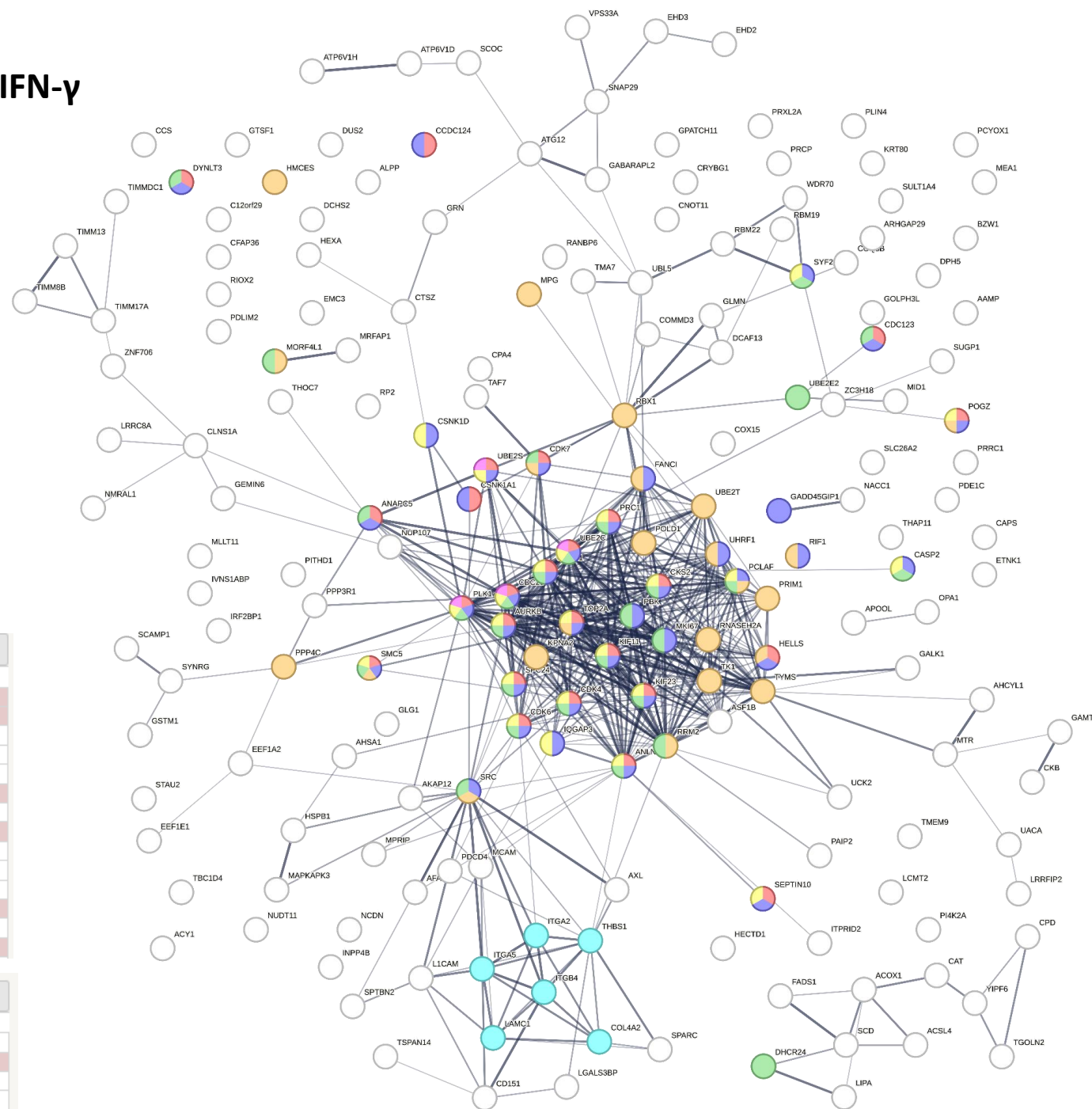
Supplementary Figure S1

Proteins upregulated (76) in A375 cells after 48h of IFN- γ

| ▼ | Biological Process (Gene Ontology) | | | | |
|------------|---|------------------|----------|------------------------|---|
| GO-term | description | count in network | strength | ▲ false discovery rate | |
| GO:0002376 | Immune system process | 47 of 2121 | 0.76 | 1.06e-22 | ● |
| GO:0019882 | Antigen processing and presentation | 18 of 93 | 1.71 | 4.18e-21 | ● |
| GO:0006955 | Immune response | 38 of 1321 | 0.88 | 5.91e-21 | ● |
| GO:0044419 | Biological process involved in interspecies interaction betw... | 38 of 1490 | 0.83 | 2.90e-19 | |
| GO:0048002 | Antigen processing and presentation of peptide antigen | 15 of 60 | 1.82 | 6.54e-19 | ● |
| GO:0051707 | Response to other organism | 36 of 1328 | 0.85 | 6.54e-19 | |
| GO:0006952 | Defense response | 36 of 1394 | 0.83 | 2.01e-18 | |
| GO:0098542 | Defense response to other organism | 30 of 989 | 0.9 | 2.01e-16 | |
| GO:0045087 | Innate immune response | 27 of 754 | 0.97 | 3.57e-16 | |
| GO:0019883 | Antigen processing and presentation of endogenous antigen | 11 of 25 | 2.06 | 7.91e-16 | |
| GO:0002483 | Antigen processing and presentation of endogenous peptid... | 10 of 18 | 2.16 | 4.84e-15 | |
| GO:0019884 | Antigen processing and presentation of exogenous antigen | 12 of 48 | 1.82 | 4.84e-15 | |
| GO:0050776 | Regulation of immune response | 27 of 844 | 0.92 | 4.84e-15 | |
| GO:0002478 | Antigen processing and presentation of exogenous peptide ... | 11 of 39 | 1.87 | 3.54e-14 | |
| GO:0002682 | Regulation of immune system process | 32 of 1438 | 0.77 | 3.54e-14 | |
| GO:0009605 | Response to external stimulus | 39 of 2355 | 0.64 | 4.38e-14 | |
| GO:0002831 | Regulation of response to biotic stimulus | 19 of 361 | 1.14 | 1.39e-13 | |
| GO:0019885 | Antigen processing and presentation of endogenous peptid... | 8 of 12 | 2.24 | 2.78e-12 | |
| GO:0002474 | Antigen processing and presentation of peptide antigen via ... | 9 of 28 | 1.93 | 8.44e-12 | |
| GO:0034097 | Response to cytokine | 23 of 804 | 0.88 | 1.56e-11 | |
| GO:0031347 | Regulation of defense response | 21 of 638 | 0.94 | 1.85e-11 | |
| GO:0045088 | Regulation of innate immune response | 15 of 238 | 1.22 | 2.00e-11 | |
| GO:0034341 | Response to interferon-gamma | 12 of 127 | 1.39 | 1.01e-10 | ● |



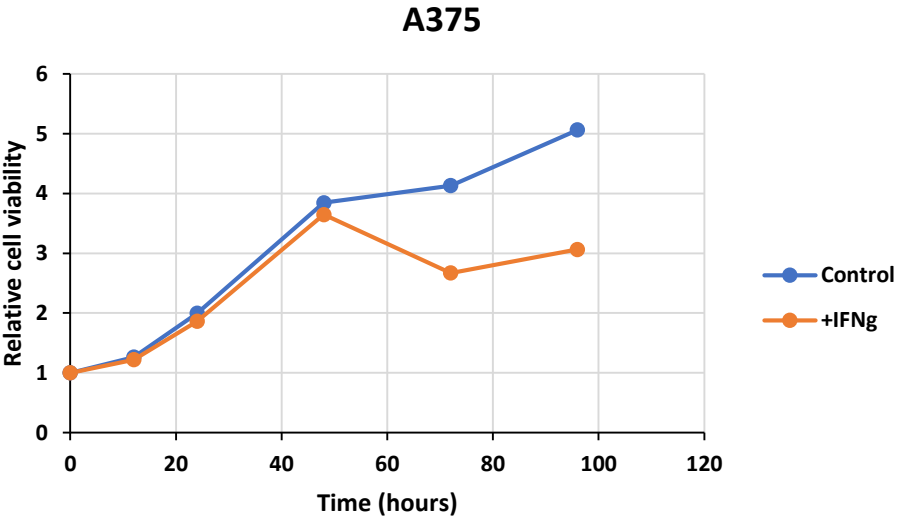
Proteins downregulated (184) in A375 cells after 48h of IFN- γ



| GO-term | description | count in network | strength | false discovery rate | |
|------------|--|------------------|----------|----------------------|---|
| GO:0051301 | Cell division | 25 of 527 | 0.69 | 1.60e-06 | 🔴 |
| GO:0007049 | Cell cycle | 37 of 1246 | 0.49 | 8.46e-06 | 🟡 |
| GO:0044237 | Cellular metabolic process | 96 of 6568 | 0.18 | 0.0033 | |
| GO:0007346 | Regulation of mitotic cell cycle | 18 of 493 | 0.58 | 0.0062 | |
| GO:1903047 | Mitotic cell cycle process | 19 of 537 | 0.57 | 0.0062 | |
| GO:0006259 | DNA metabolic process | 23 of 785 | 0.48 | 0.0071 | 🟡 |
| GO:0000278 | Mitotic cell cycle | 20 of 631 | 0.52 | 0.0077 | |
| GO:0051726 | Regulation of cell cycle | 28 of 1108 | 0.42 | 0.0077 | 🟢 |
| GO:0008152 | Metabolic process | 108 of 7988 | 0.15 | 0.0077 | |
| GO:0051983 | Regulation of chromosome segregation | 9 of 128 | 0.87 | 0.0094 | |
| GO:1901990 | Regulation of mitotic cell cycle phase transition | 14 of 332 | 0.64 | 0.0094 | |
| GO:0022402 | Cell cycle process | 23 of 835 | 0.46 | 0.0096 | 🟡 |
| GO:0071704 | Organic substance metabolic process | 102 of 7522 | 0.15 | 0.0103 | |
| GO:1904668 | Positive regulation of ubiquitin protein ligase activity | 4 of 11 | 1.58 | 0.0111 | 🟡 |

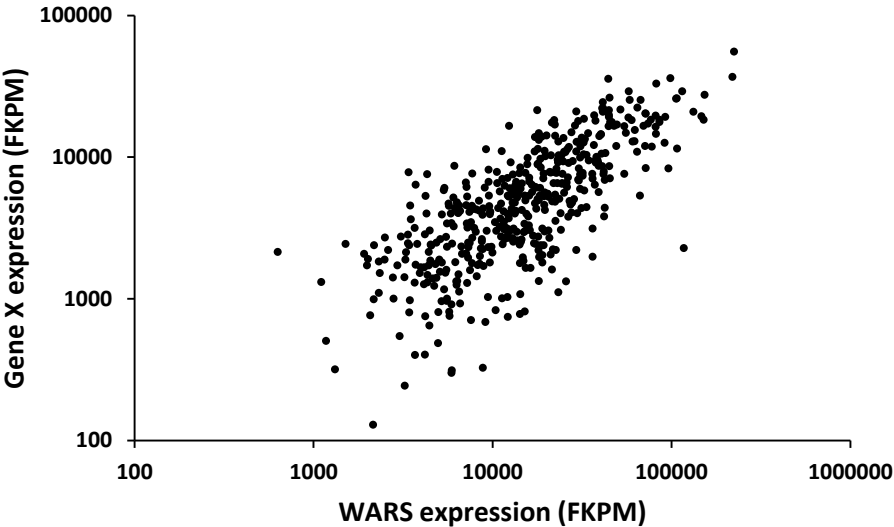
| KEGG Pathways | | | | |
|----------------|--------------------------------|-------------------------|-----------------|-----------------------------|
| <i>pathway</i> | <i>description</i> | <i>count in network</i> | <i>strength</i> | <i>false discovery rate</i> |
| hsa04110 | Cell cycle | 8 of 120 | 0.84 | 0.0104 |
| hsa04512 | ECM-receptor interaction | 6 of 88 | 0.85 | 0.0465 |
| hsa05222 | Small cell lung cancer | 6 of 92 | 0.83 | 0.0465 |
| hsa04120 | Ubiquitin mediated proteolysis | 7 of 134 | 0.74 | 0.0465 |

Supplementary Figure S3



TCGA and Gtex data (Tumors and normal tissues)

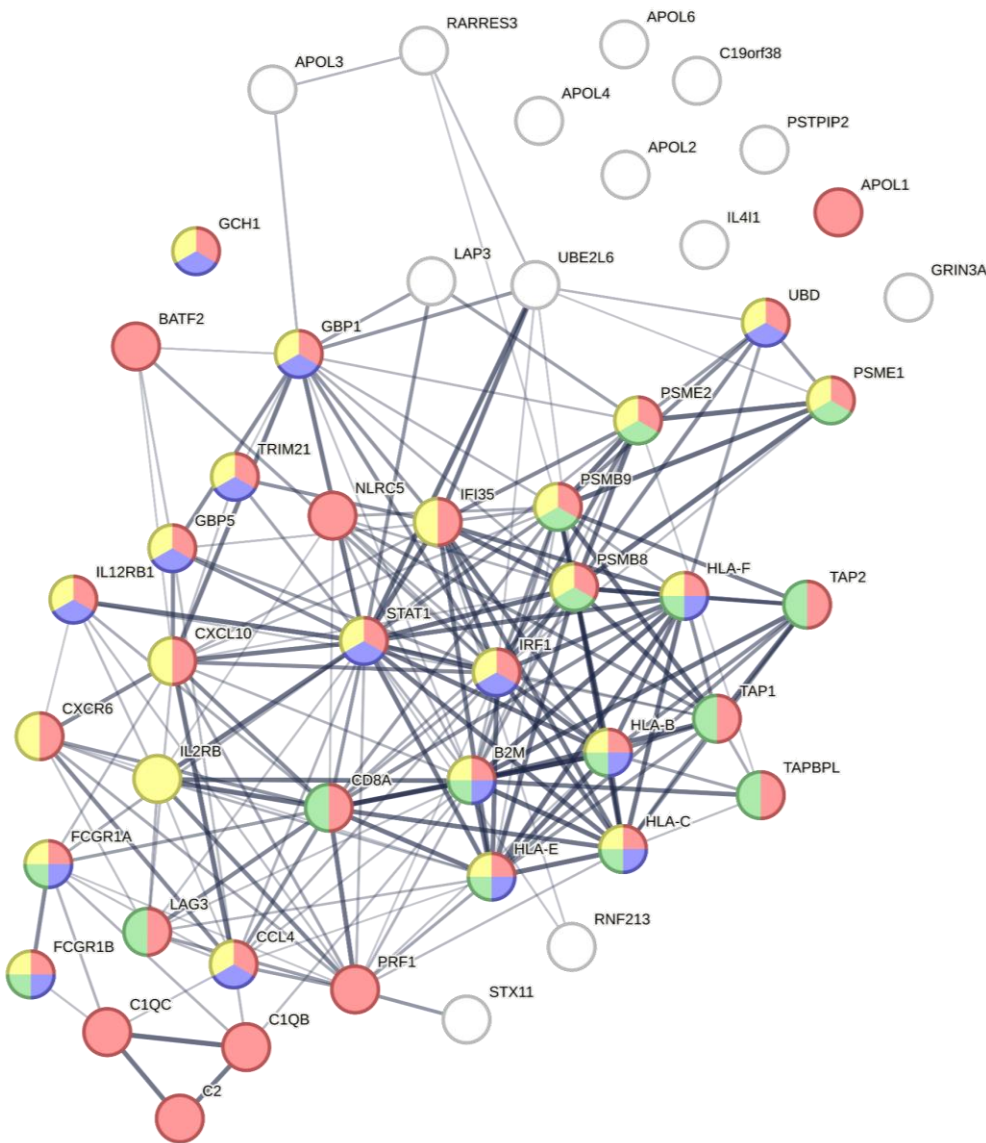
Comparison of the expression profile of WARS and all the genes from TCGA and Gtex (cuff-off = Top 50 correlating genes)



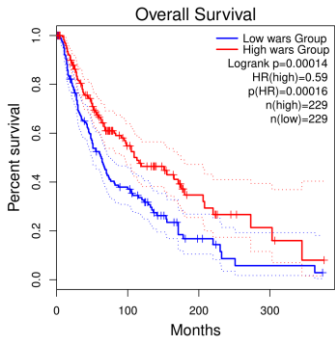
Top 50 correlating genes correlating with WARS

| Gene Symbol | Gene ID | PCC |
|-------------|--------------------|------|
| TAP1 | ENSG00000168394.10 | 0.65 |
| STAT1 | ENSG00000115415.18 | 0.59 |
| TAP2 | ENSG00000204267.13 | 0.58 |
| GBP5 | ENSG00000154451.14 | 0.58 |
| BATF2 | ENSG00000168062.9 | 0.56 |
| LAP3 | ENSG0000002549.12 | 0.53 |
| GBP1 | ENSG00000117228.9 | 0.51 |
| CXCL11 | ENSG00000169246.12 | 0.49 |
| GBP4 | ENSG00000162654.8 | 0.49 |
| GBP1P1 | ENSG00000225452.6 | 0.48 |
| PSMB9 | ENSG00000240065.7 | 0.48 |
| UBE2L6 | ENSG00000156587.15 | 0.48 |
| ETV7 | ENSG00000010030.13 | 0.47 |
| CXCL9 | ENSG00000138755.5 | 0.47 |
| CXCL10 | ENSG00000169245.5 | 0.46 |
| HLA-A | ENSG00000206503.11 | 0.45 |
| LAG3 | ENSG00000089692.8 | 0.45 |
| EPSTI1 | ENSG00000133106.14 | 0.45 |
| APOL6 | ENSG00000221963.5 | 0.44 |
| PSMB8 | ENSG00000204264.8 | 0.44 |
| IL15BP | ENSG00000137456.17 | 0.43 |
| IFI35 | ENSG00000068079.7 | 0.43 |
| TRIM21 | ENSG00000132109.9 | 0.43 |

Supplementary Figure S5



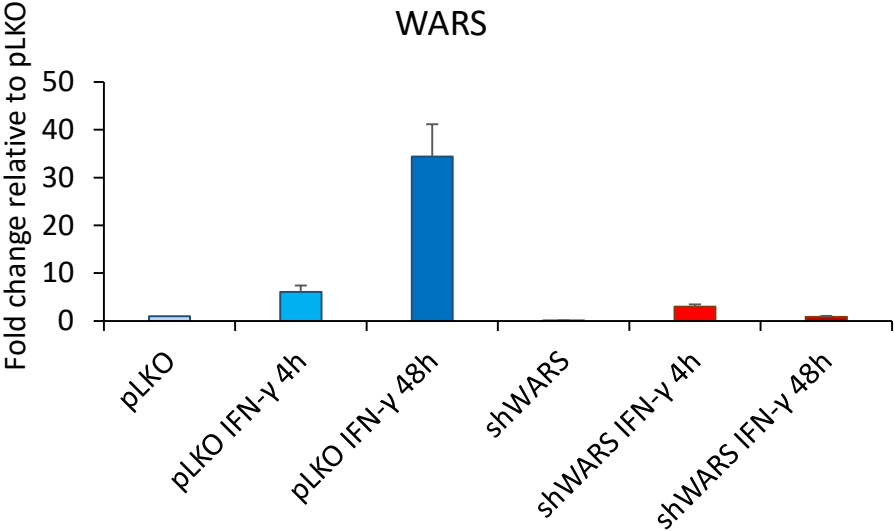
Patient survival



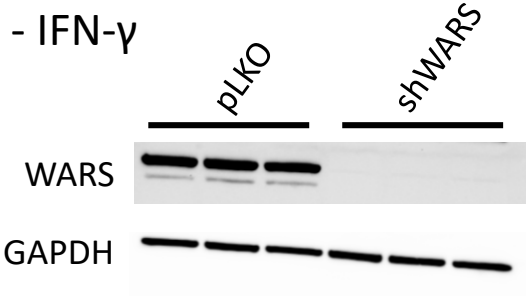
| Study Name | Study Abbreviation |
|--|--------------------|
| Adenoid cystic carcinoma | ACC |
| Bladder Carcinoma | BLCA |
| Breast cancer | BRCA |
| Cervical Squamous Cell Carcinoma and Endocervical Adenocarcinoma | CESC |
| Cholangiocarcinoma | CHOL |
| Colon Adenocarcinoma | COAD |
| Lymphoid Neoplasm Diffuse Large B-cell Lymphoma | DLBC |
| Esophageal Carcinoma | ESCA |
| Glioblastoma multiforme | GBM |
| Head-Neck Squamous Cell Carcinoma | HNSC |
| Kidney Chromophobe | KICH |
| Kidney Renal Clear Cell Carcinoma | KIRC |
| Cervical Kidney renal papillary cell carcinoma | KIRP |
| Acute Myeloid Leukemia | LAML |
| Low Grade Glioma | LGG |
| Liver Hepatocellular Carcinoma | LIHC |
| Lung Adenocarcinoma | LUAD |
| Lung Squamous Cell Carcinoma | LUSC |
| Mesothelioma | MESO |
| Ovarian Cancer | OV |
| Pancreatic Ductal Adenocarcinoma | PAAD |
| Pheochromocytoma and Paraganglioma | PCPG |
| Prostate adenocarcinoma | PRAD |
| Rectum Adenocarcinoma | READ |
| Sarcoma | SARC |
| Skin cutaneous melanoma | SKCM |
| Stomach Adenocarcinoma | STAD |
| Testicular Germ Cell Tumors | TGCT |
| Thyroid carcinoma | THCA |
| Thymoma | THYM |
| Uterine Corpus Endometrial Carcinoma | UCEC |
| Uterine Carcinosarcoma | UCS |
| Uveal Melanoma | UVM |

Supplementary Figure S6

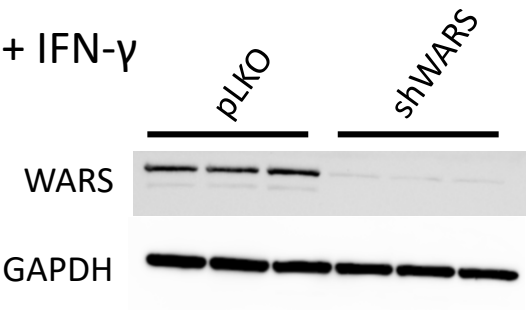
A



B



C



Supplementary Figure S1: Proteins up-regulated in A375 cells following interferon- γ treatment and enriched pathways.

Supplementary Figure S2: Proteins down-regulated in A375 cells following interferon- γ treatment and enriched pathways.

Supplementary Figure S3: Cell viability assay of A375 cells treated with vehicle or interferon- γ . 5,000 A375 cells were seeded in white 96-well plates and treated with 100ng/mL of IFN- γ . Cell viability was monitored every 24h for 4 days using Cell Titer Glo kit (Promega).

Supplementary Figure S4: Identification of genes correlating with *WARS* using GEPIA.

Supplementary Figure S5: Cancer patients survival analysis of genes correlating with *WARS* using GEPIA.

Supplementary Figure S6: Inhibition of *WARS* expression by shRNA at the RNA (A) and protein (B-C) levels in A375 cells treated with vehicle (-IFN- γ) or interferon- γ (+IFN- γ).