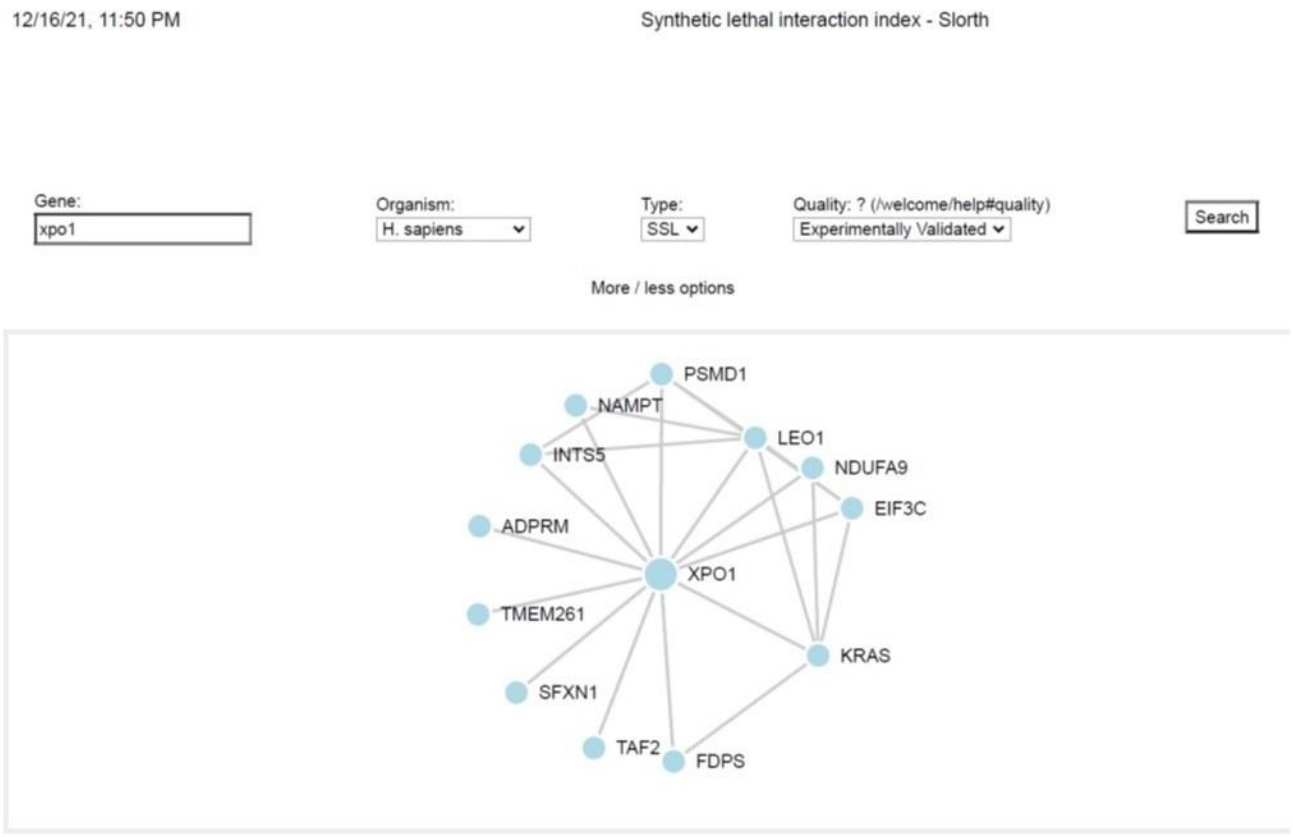
**Supplementary Figure 1.**



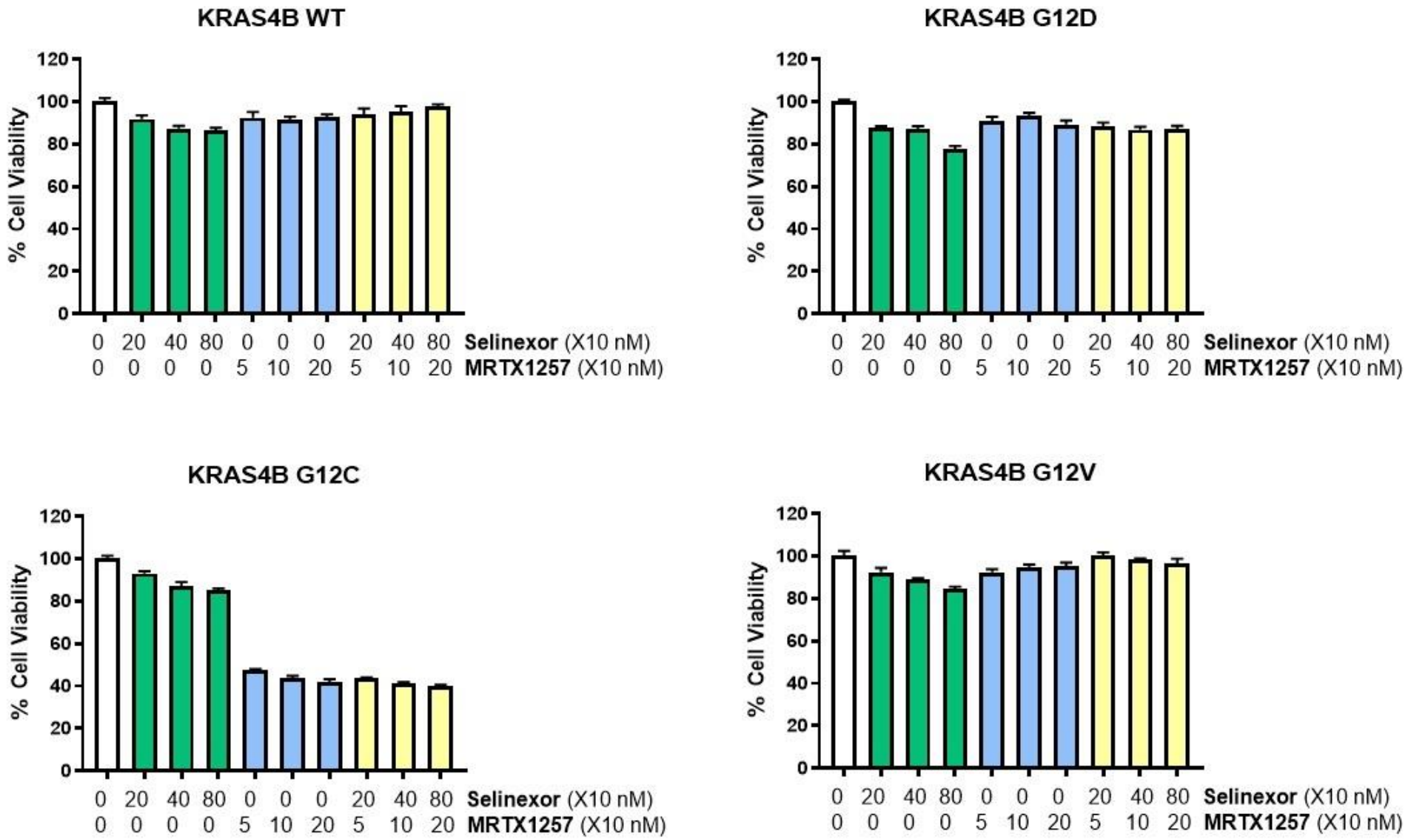

## Interactions

| Gene ID A | Gene name A | Gene ID B | Gene name B | Organism | Type | Source | Score ? (/welcome/help#score) | |
|---|---|---|---|---|---|---|---|---|
| ENSG00000139180 | NDUFA9 (/genes/649) | ENSG00000082898 | XPO1 (/genes/1061) | H. sapiens | SSL | BioGRID | 1.0 | View (/interactions/3334) |
| ENSG00000166477 | LEO1 (/genes/540) | ENSG00000082898 | XPO1 (/genes/1061) | H. sapiens | SSL | BioGRID | 1.0 | View (/interactions/2858) |
| ENSG00000173692 | PSMD1 (/genes/754) | ENSG00000082898 | XPO1 (/genes/1061) | H. sapiens | SSL | BioGRID | 1.0 | View (/interactions/3644) |
| ENSG00000164466 | SFXN1 (/genes/830) | ENSG00000082898 | XPO1 (/genes/1061) | H. sapiens | SSL | BioGRID | 1.0 | View (/interactions/3908) |
| ENSG00000170222 | ADPRM (/genes/30) | ENSG00000082898 | XPO1 (/genes/1061) | H. sapiens | SSL | BioGRID | 1.0 | View (/interactions/82) |
| ENSG00000184110 | EIF3C (/genes/322) | ENSG00000082898 | XPO1 (/genes/1061) | H. sapiens | SSL | BioGRID | 1.0 | View (/interactions/1686) |
| ENSG00000064313 | TAF2 (/genes/867) | ENSG00000082898 | XPO1 (/genes/1061) | H. sapiens | SSL | BioGRID | 1.0 | View (/interactions/3999) |
| ENSG00000185085 | INTS5 (/genes/492) | ENSG00000082898 | XPO1 (/genes/1061) | H. sapiens | SSL | BioGRID | 1.0 | View (/interactions/2488) |
| ENSG00000137038 | TMEM261 (/genes/881) | ENSG00000082898 | XPO1 (/genes/1061) | H. sapiens | SSL | BioGRID | 1.0 | View (/interactions/4031) |
| ENSG00000133703 | KRAS (/genes/7) | ENSG00000082898 | XPO1 (/genes/1061) | H. sapiens | SSL | BioGRID | 1.0 | View (/interactions/2767) |
| ENSG00000105835 | NAMPT (/genes/642) | ENSG00000082898 | XPO1 (/genes/1061) | H. sapiens | SSL | BioGRID | 1.0 | View (/interactions/3305) |
| ENSG00000160752 | FDPS (/genes/383) | ENSG00000082898 | XPO1 (/genes/1061) | H. sapiens | SSL | BioGRID | 1.0 | View (/interactions/2038) |

slorth.biochem.sussex.ac.uk/interactions?utf8=✓&gene=xpo1&organism=H.+sapiens&interaction_type=SSL&score_filter=1&commit=Search&disease... 1/2

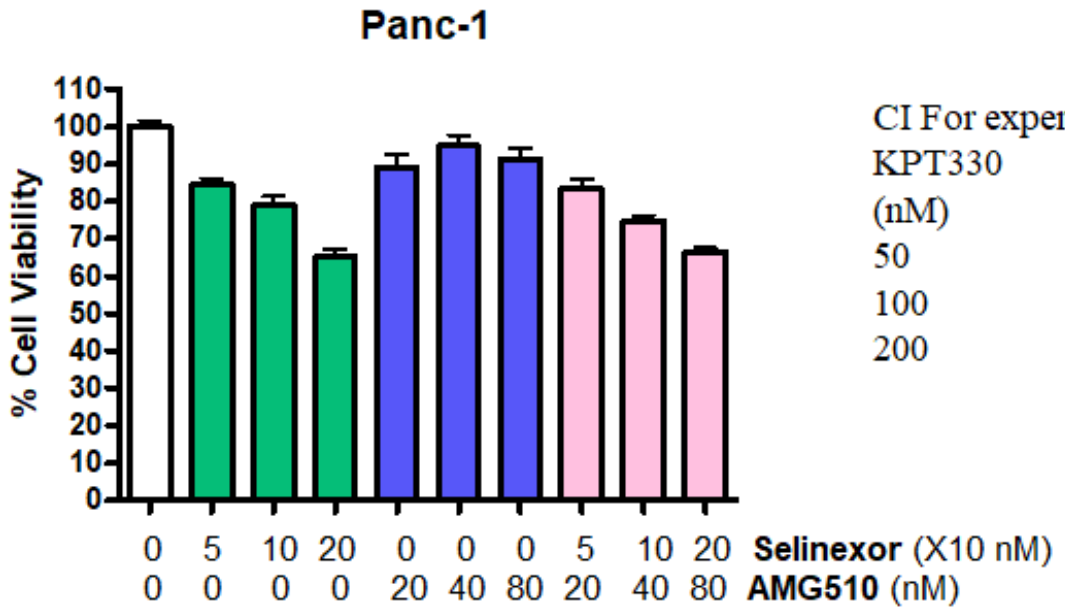
XPO1-KRAS synthetic lethal interaction identified using the Slorth database (http://slorth.biochem.sussex.ac.uk/welcome/index)

**Supplementary Figure 2.**




KRAS WT, KRAS G12D and KRAS G12V MEF cell lines were refractory to growth inhibition by selinexor or MRTX1257 or their combinations. However, only KRAS4B G12C cells responded to KRAS G12C inhibitor MRTX1257.

**Supplementary Figure 3.**

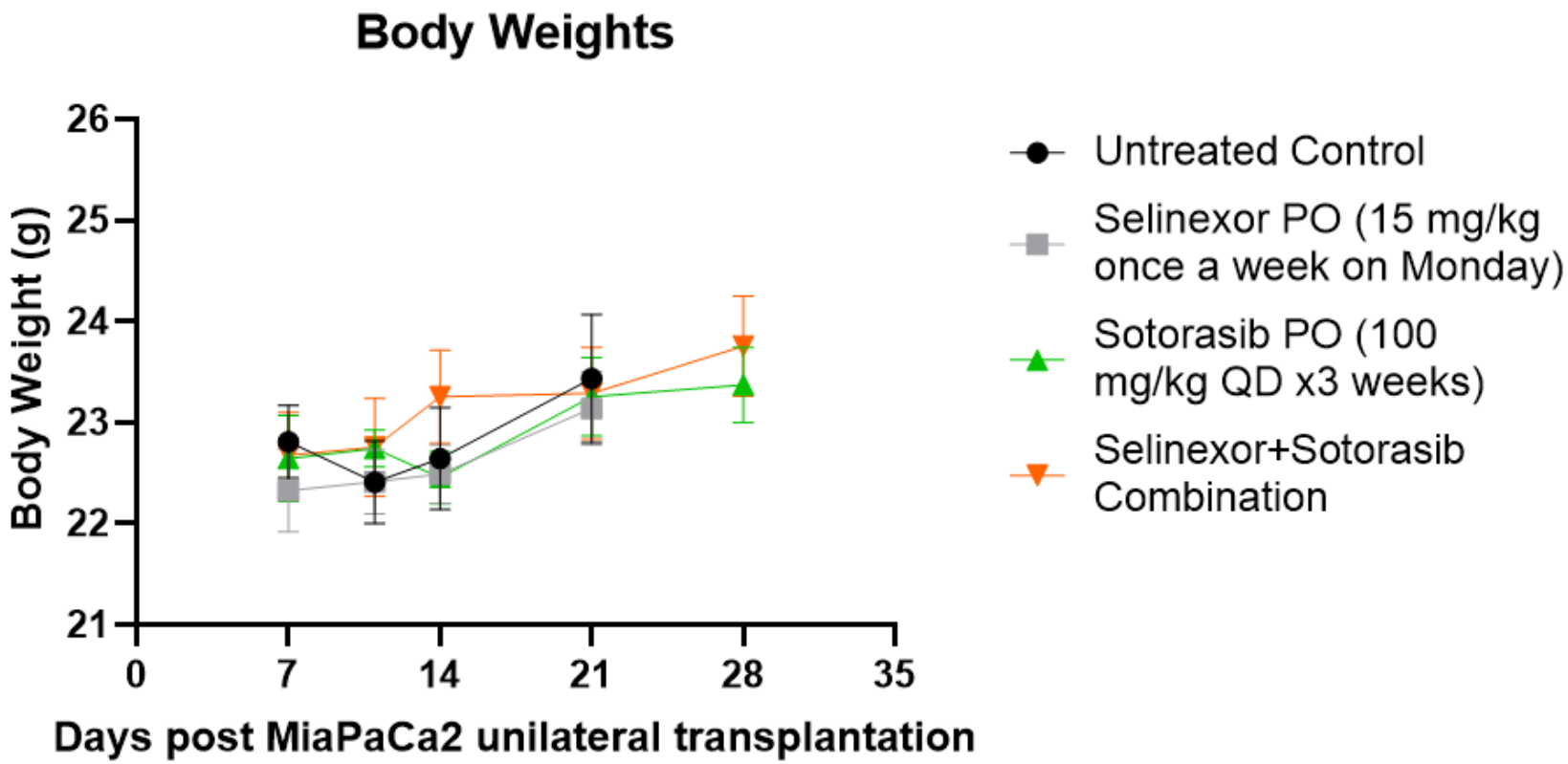



CI For experimental values

| KPT330 (nM) | AMG510 (nM) | Fa | CI |
|---|---|---|---|
| 50 | 20 | 0.168122 | 72.761 |
| 100 | 40 | 0.251687 | 2706.794 |
| 200 | 80 | 0.335186 | 5.57e+004 |

KRAS G12D mutant PDAC cell line Panc-1 was refractory to growth inhibition by KRAS G12C inhibitor AMG510. Treatment of Panc-1 cells with combinations of selinexor and AMG510, did not show any synergistic effect (CI > 1).

**Supplementary Figure 4.**




Body weights of mice xenografted with MiaPaCa2 tumors were measured during the treatment period. Neither of the drugs, either as single agent or in combination, induced any loss of body weight.

**Supplementary Table 1.** Sequences of primers used

| Primers | Sequences | |
|---|---|---|
| KRAS | *Forward* | GTGCAAGAGAGCTGAGGGAG |
| | *Reverse* | ATGCTGGTGGGACAGAAGTG |
| XPO1 | *Forward* | GGAAAACTGTGAAACCCACCTT |
| | *Reverse* | GCTGCATGGTCTGCTAACAT |
| Erk2 | *Forward* | ATTACGACCCGAGTGACGAG |
| | *Reverse* | GATGTCTGAGCACGTCCAGT |
| Bcl-2 | *Forward* | TGAACTGGGGGAGGATTGTG |
| | *Reverse* | CGTACAGTTCCACAAAGGCA |
| β-actin | *Forward* | GCACAGAGCCTCGCCTT |
| | *Reverse* | TCATCATCCATGGTGAGCTG |
| 18S | *Forward* | GCAATTATTCCCCATGAACG |
| | *Reverse* | GGCCTCACTAAACCATCCAA |

**Supplementary Table 2.** Combination Index (CI) values at various dose combinations of the drugs tested on different KRAS G12C mutant cell lines (MiaPaCa-2, NCI-H2122 and KRAS4B G12C)

| ***MiaPaCa-2*** | | |
|---|---|---|
| **Selinexor (nM)** | **AMG510 (nM)** | **CI** |
| 50 | 20 | 0.927 |
| 100 | 40 | 1.162 |
| 200 | 80 | 1.554 |
| ***NCI-H2122*** | | |
| **Selinexor (nM)** | **AMG510 (nM)** | **CI** |
| 150 | 50 | 0.986 |
| 300 | 100 | 0.931 |
| 600 | 200 | 0.781 |
| ***KRAS4B G12C*** | | |
| **Selinexor (nM)** | **MRTX1257 (nM)** | **CI** |
| 200 | 50 | 0.41 |
| 400 | 100 | 0.451 |
| 800 | 200 | 0.627 |
| ***KRAS4B G12C*** | | |
| **Selinexor (nM)** | **AMG510 (nM)** | **CI** |
| 800 | 800 | 0.103 |