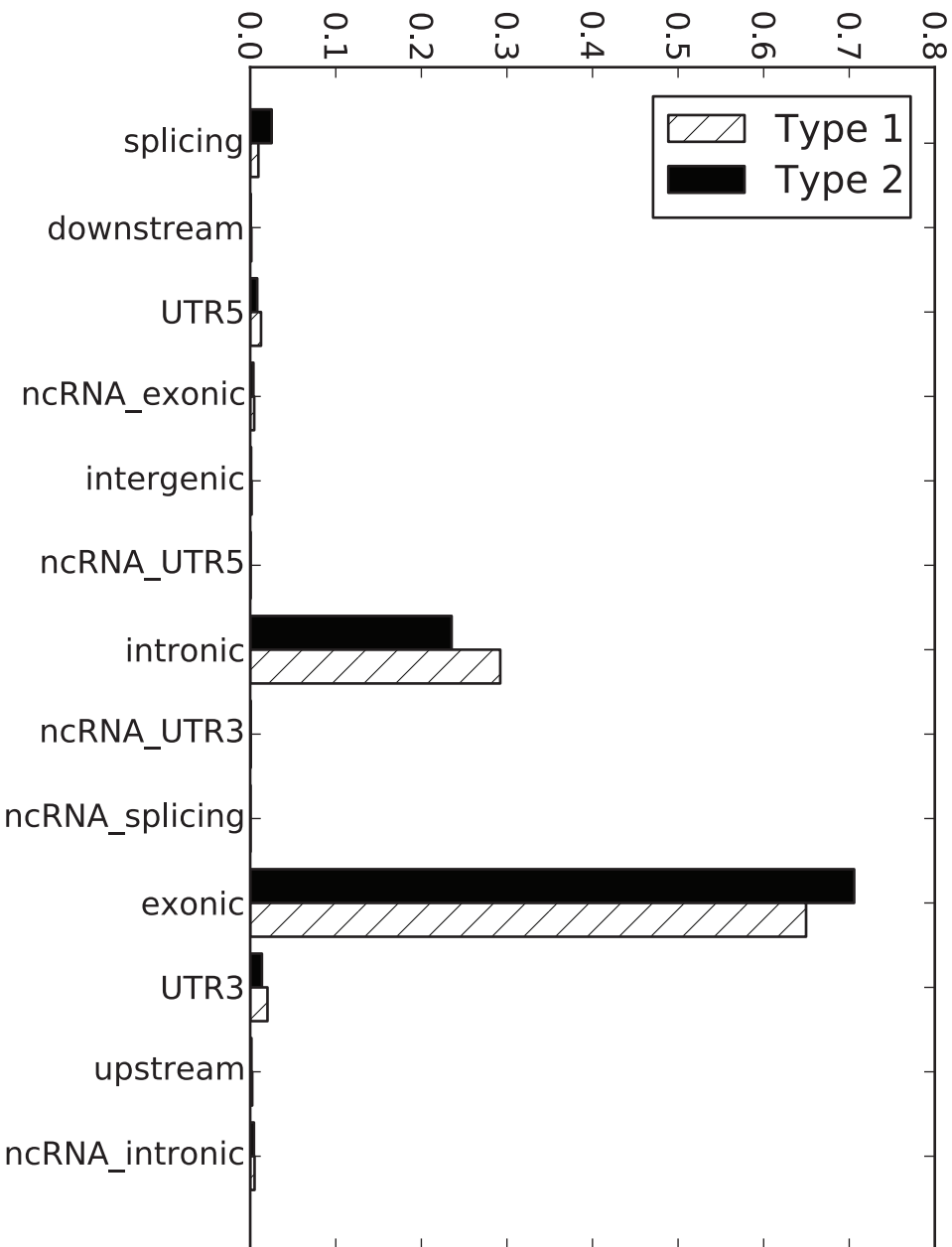


FIGURE S1

**A**

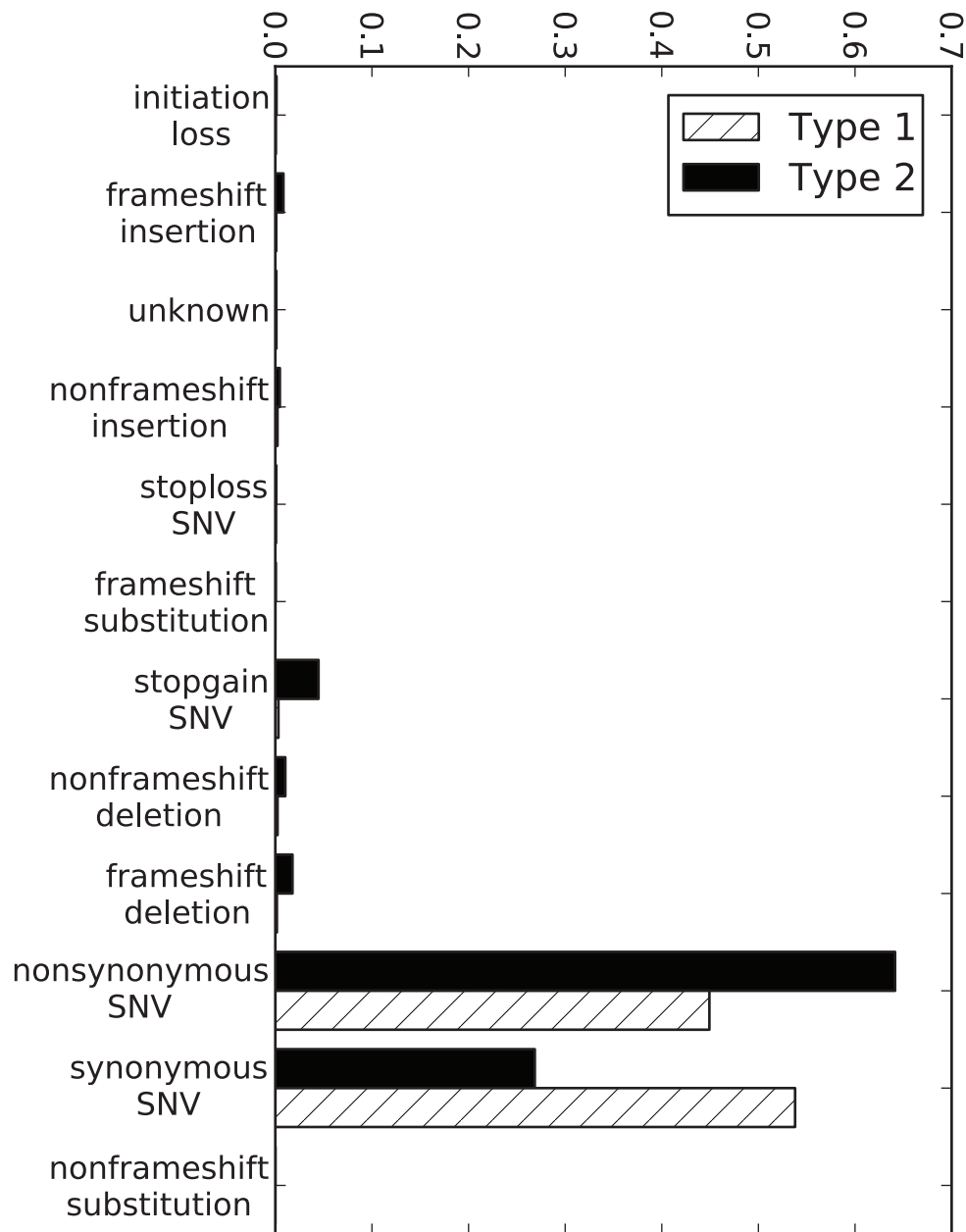
## Distribution of Variants by Genomic Annotation

Fraction of variants

**B**

## Distribution of Variants by Exonic Annotation

Fraction of variants



## **The NCI-60 Cell Line Panel**

| <b>Cell Line</b> | <b>Tissue</b> | <b>MSI (*)</b> |
|------------------|---------------|----------------|
| 786-0            | Renal         | Negative       |
| A498             | Renal         | Negative       |
| A549 ATCC        | Lung          | Negative       |
| ACHN             | Renal         | Negative       |
| BT-549           | Breast        | Negative       |
| CAKI-1           | Renal         | Negative       |
| CCRF-CEM         | Leukemia      | POSITIVE       |
| COLO-205         | Colon         | Negative       |
| DU145            | Prostate      | POSTIVE        |
| EKVX             | Lung          | Negative       |
| HCC-2998         | Colon         | Negative       |
| HCT-116          | Colon         | POSITIVE       |
| HCT-15           | Colon         | POSITIVE       |
| HL-60            | Leukemia      | Negative       |
| HOP-62           | Lung          | Negative       |
| HOP-92           | Lung          | Negative       |
| Hs-578T          | Breast        | Negative       |
| HT29             | Colon         | Negative       |
| IGR-OV1          | Ovarian       | POSITIVE       |
| K562             | Leukemia      | Negative       |
| KM12             | Colon         | POSITIVE       |
| LOX IMVI         | Melanoma      | NA             |
| M14              | Melanoma      | Negative       |
| MALME-3M         | Melanoma      | Negative       |
| MCF-7            | Breast        | Negative       |
| MDA-MB-231       | Breast        | Negative       |
| MDA-MB-435       | Melanoma      | Negative       |
| MDA-MB-468       | Breast        | Negative       |
| MDA-N (1)        | Melanoma      | NA             |
| MOLT-4           | Leukemia      | POSITIVE       |

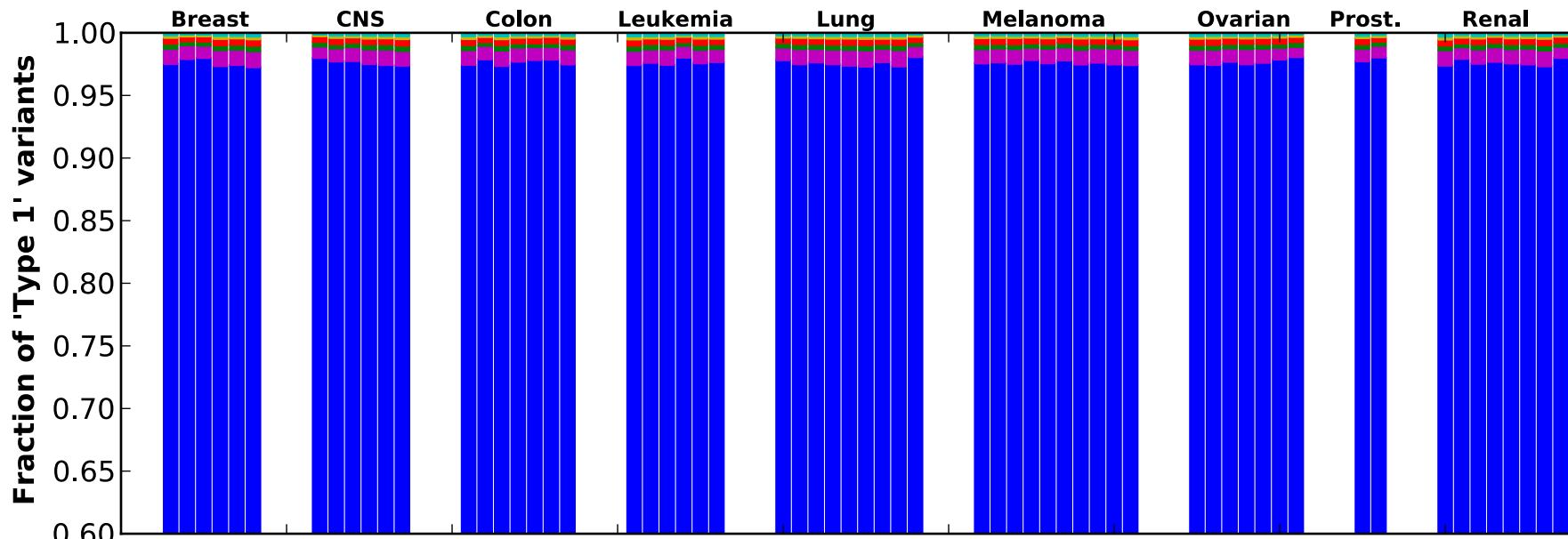
| <b>Cell Line</b> | <b>Tissue</b> | <b>MSI (*)</b> |
|------------------|---------------|----------------|
| NCI-H226         | Lung          | Negative       |
| NCI-H23          | Lung          | Negative       |
| NCI-H322M        | Lung          | Negative       |
| NCI-H460         | Lung          | Negative       |
| NCI-H522         | Lung          | Negative       |
| NCI/ADR-RES      | Ovarian       | Negative       |
| OVCAR-3          | Ovarian       | Negative       |
| OVCAR-4          | Ovarian       | Negative       |
| OVCAR-5          | Ovarian       | Negative       |
| OVCAR-8          | Ovarian       | Negative       |
| PC-3             | Prostate      | Negative       |
| RPMI-8226        | Leukemia      | Negative       |
| RXF-393          | Renal         | Negative       |
| SF-268           | CNS           | Negative       |
| SF-295           | CNS           | Negative       |
| SF-539           | CNS           | Negative       |
| SK-MEL-2         | Melanoma      | POSITIVE       |
| SK-MEL-28        | Melanoma      | Negative       |
| SK-MEL-5         | Melanoma      | Negative       |
| SK-OV-3          | Ovarian       | POSITIVE       |
| SN12C            | Renal         | Negative       |
| SNB-19           | CNS           | Negative       |
| SNB-75           | CNS           | Negative       |
| SR               | Leukemia      | Negative       |
| SW-620           | Colon         | Negative       |
| T-47D            | Breast        | Negative       |
| TK-10            | Renal         | Negative       |
| U251             | CNS           | Negative       |
| UACC-257         | Melanoma      | Negative       |
| UACC-62          | Melanoma      | Negative       |
| UO-31            | Renal         | Negative       |

\* MSI status has been collect from the data in the COSMIC database.  
 (<http://www.sanger.ac.uk/genetics/CGP/MSI/table1.shtml>)

FIGURE S3

# Distribution of Variants by Type

**A**



**B**

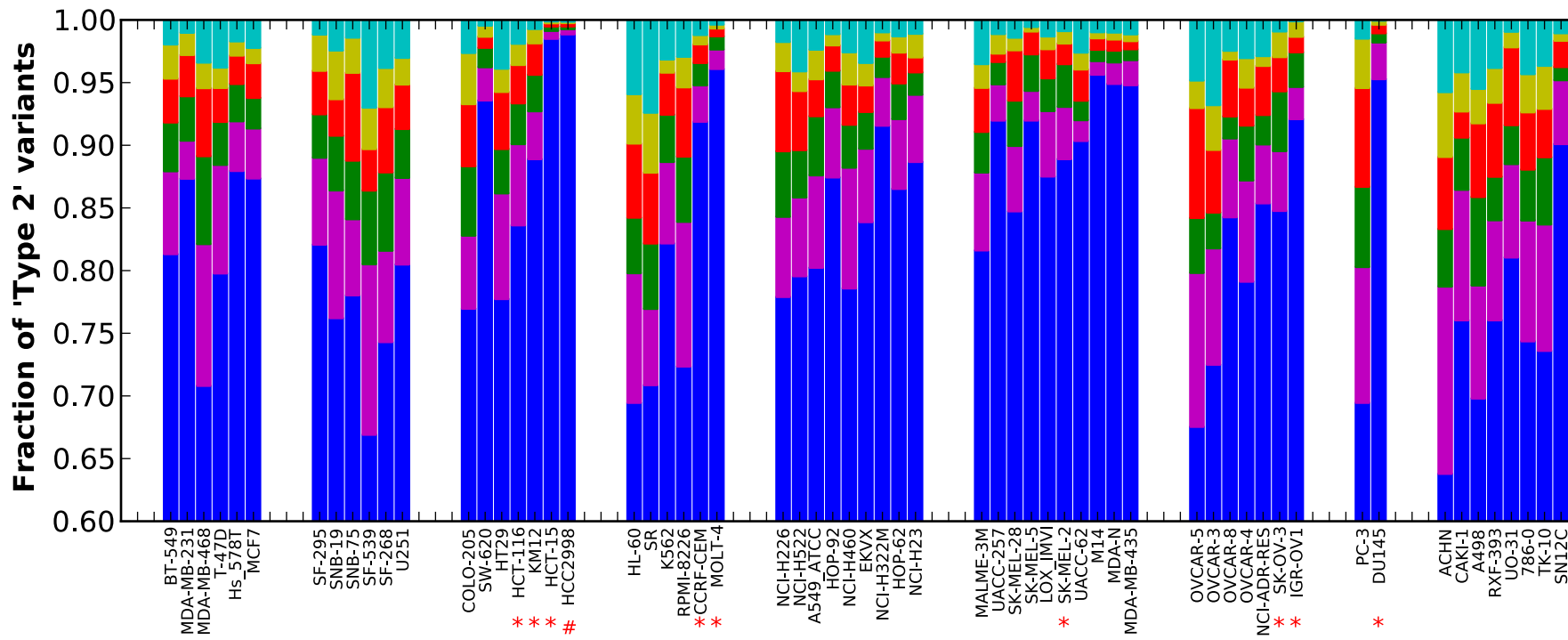


FIGURE S4

CLUSTAL 2.1 MULTIPLE SEQUENCE ALIGNMENT

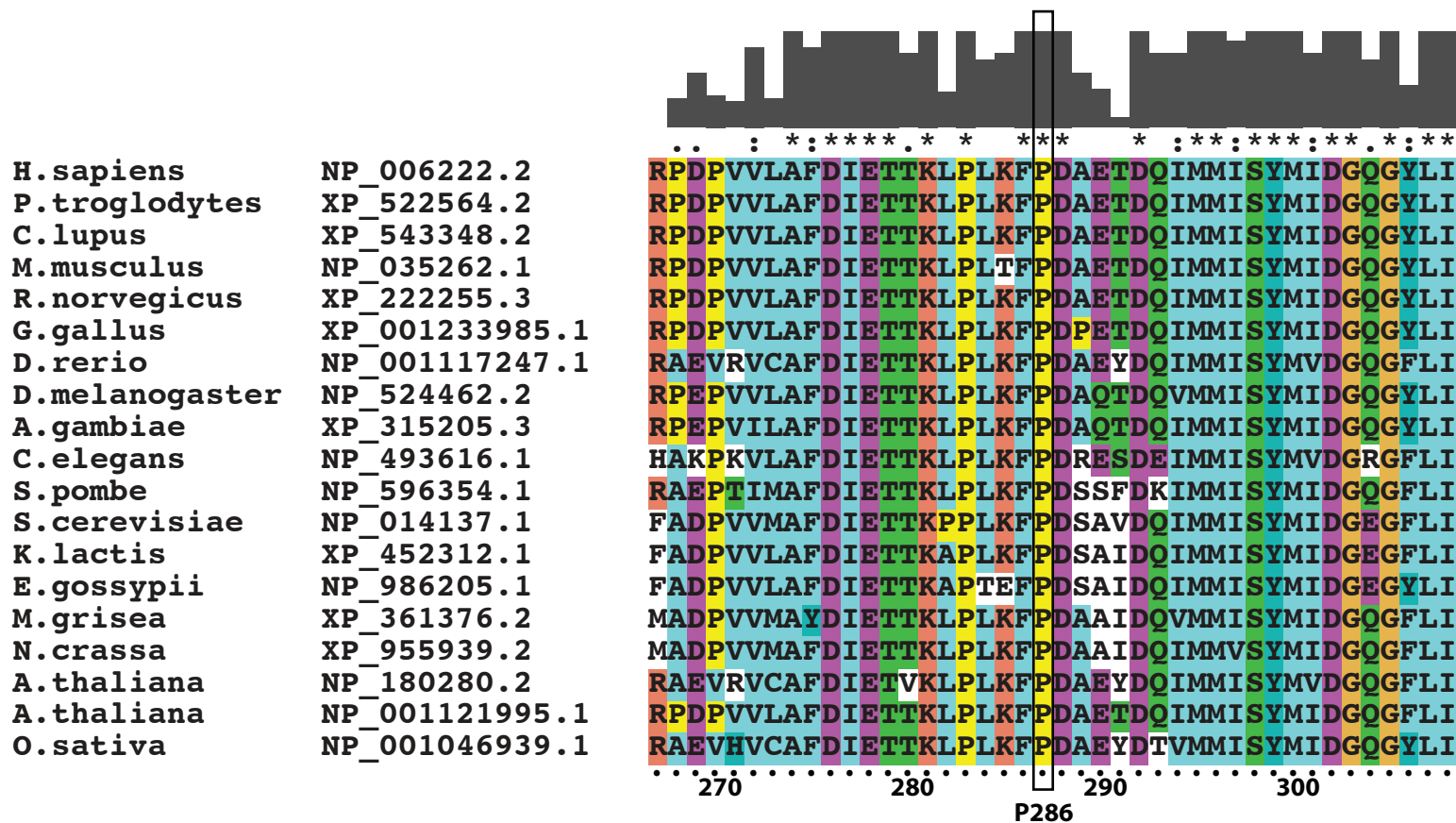


FIGURE S5

**Filter Cascade**

Variants: 158398 | Genes: 16688

- Keep Only NCI Type2 from... (53912 Variants, 14073 Genes)
- Common Variants (53689 Variants, 14070 Genes)
- Predicted Deleterious (14643 Variants, 8268 Genes)
- Genetic Analysis (14643 Variants, 8268 Genes)
- Cancer Driver Variants (7490 Variants, 4148 Genes)
- Biological Context: ERK... (204 Variants, 102 Genes)

Add Filter

Edit Columns | Export | Create List | Search for gene name/symbol | 204 variants

| Chr... | Position  | Gene Region    | Gene Sym... | Protein Variant | Case Samples | Translation Impact | SIFT Functio... | Regulatory Site | Regulator | Variant Findings | dbSNP ID | File 1: NCIType2.bed |
|--------|-----------|----------------|-------------|-----------------|--------------|--------------------|-----------------|-----------------|-----------|------------------|----------|----------------------|
| 11     | 108115681 | Exonic         | ATM         | E277X           |              | stop gain          |                 |                 |           |                  |          | 1.0                  |
| 11     | 108115600 | Exonic         | ATM         | R250X           |              | stop gain          |                 |                 |           | 1                |          | 1.0                  |
| 11     | 108160407 | Exonic         | ATM         | L1439I          |              | nonsynonymous      | Damaging        |                 |           |                  |          | 1.0                  |
| 11     | 108224578 | Exonic         | ATM         | G2919G          |              | synonymous         |                 |                 |           | 1                |          | 1.0                  |
| 11     | 108213965 | Exonic         | ATM         | Q2762R          |              | nonsynonymous      | Damaging        |                 |           |                  |          | 1.0                  |
| 11     | 108200941 | Exonic         | ATM         | R2436S          |              | nonsynonymous      | Damaging        |                 |           |                  |          | 1.0                  |
| 11     | 108192069 | Exonic         | ATM         | S2165F          |              | nonsynonymous      | Damaging        |                 |           |                  |          | 1.0                  |
| 11     | 108115595 | Exonic         | ATM         | R248Q           |              | nonsynonymous      | Damaging        |                 |           |                  |          | 1.0                  |
| 7      | 140453136 | Exonic         | BRAF        | V600E           |              | nonsynonymous      | Damaging        |                 |           | 1766             | 11348802 | 1.0                  |
| 7      | 140481417 | Exonic         | BRAF        | G464V           |              | nonsynonymous      | Damaging        |                 |           | 10               | 12191334 | 1.0                  |
| 7      | 28843879  | Exonic         | CREB5       | G117X, G223X,   |              | stop gain          |                 |                 |           |                  |          | 1.0                  |
| 8      | 29194590  | Exonic         | DUSP4       | S289C, S380C    |              | nonsynonymous      | Damaging        |                 |           |                  |          | 1.0                  |
| 12     | 89743278  | Exonic         | DUSP6       | S154L, S300L    |              | nonsynonymous      | Damaging        |                 |           |                  |          | 1.0                  |
| 13     | 41517270  | Exonic         | ELF1        | I184M, I208M    |              | nonsynonymous      | Damaging        |                 |           |                  |          | 1.0                  |
| 1      | 201984443 | Exonic         | ELF3        | R370W           |              | nonsynonymous      | Damaging        |                 |           |                  |          | 1.0                  |
| 1      | 201981111 | Exonic         | ELF3        | P64T            |              | nonsynonymous      | Damaging        |                 |           |                  |          | 1.0                  |
| 1      | 201980265 | Exonic         | ELF3        | M1V             |              | nonsynonymous      | Damaging        |                 |           |                  |          | 1.0                  |
| 11     | 34515223  | Exonic, Intron | ELF5        | Y53C, Y63C      |              | nonsynonymous      | Damaging        |                 |           |                  |          | 1.0                  |
| 11     | 34501786  | Exonic         | ELF5        | W155fs*, W182f  |              | frameshift         |                 |                 |           |                  |          | 1.0                  |
| 10     | 128974513 | Exonic, Intron | DOCK1, FAM1 | F49L            |              | nonsynonymous      | Damaging        |                 |           |                  |          | 1.0                  |
| 10     | 128973581 | Exonic, Intron | DOCK1, FAM1 | A360V           |              | nonsynonymous      | Damaging        |                 |           |                  |          | 1.0                  |
| 10     | 128973815 | Exonic, Intron | DOCK1, FAM1 | C282Y           |              | nonsynonymous      | Damaging        |                 |           |                  |          | 1.0                  |
| 14     | 75747842  | Exonic         | FOS         | S288fs*         |              | frameshift         |                 |                 |           |                  |          | 1.0                  |
| 14     | 75747626  | Exonic         | FOS         | M216fs*         |              | frameshift         |                 |                 |           |                  |          | 1.0                  |
| 14     | 75747369  | Exonic         | FOS         | A167V           |              | nonsynonymous      | Damaging        |                 |           |                  |          | 1.0                  |
| 6      | 112017542 | Exonic         | FYN         | V272A, V324A, V |              | nonsynonymous      | Damaging        |                 |           |                  |          | 1.0                  |
| 6      | 111982995 | Exonic         | FYN         | E466K, E518K,   |              | nonsynonymous      | Damaging        |                 |           |                  |          | 1.0                  |
| 11     | 533535    | Exonic         | HRAS        | R123H           |              | nonsynonymous      | Damaging        |                 |           |                  |          | 1.0                  |
| 11     | 534288    | Exonic         | HRAS        | G12D            |              | nonsynonymous      | Damaging        |                 |           | 38               | 10480423 | 1.0                  |

**Legend [hide]**

Function

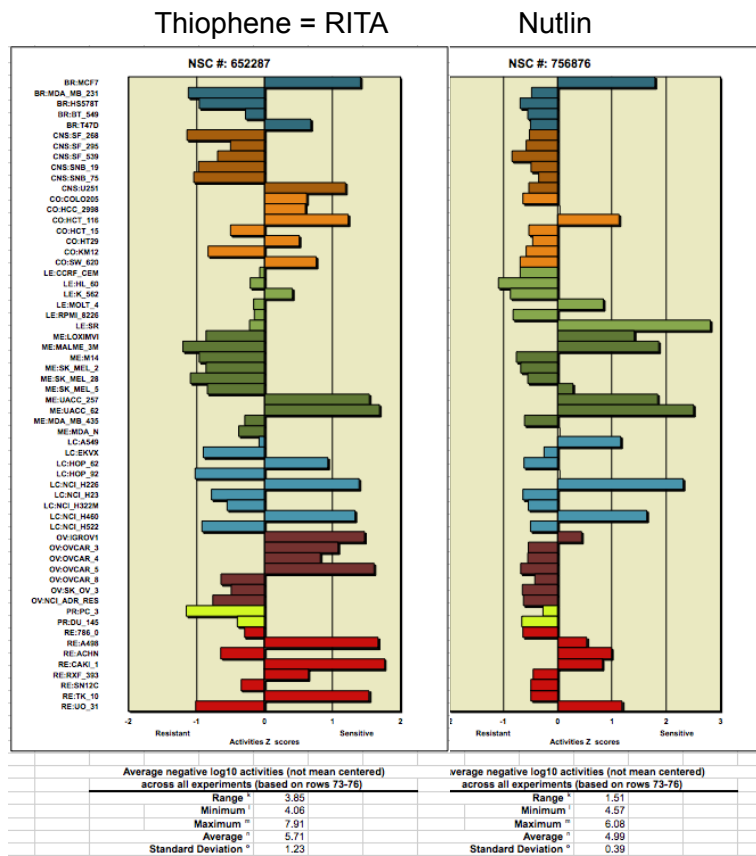
Call Quality <20 ..... 30+

loss normal gain

- Identical to Reference Genome
- Heterozygous Variant
- Heterozygous/Ambiguous
- Homozygous Variant
- Copy Number Gain/Heterozygous
- Copy Number Gain/Homozygous
- Hemizygous
- Nullizygous
- Gene Fusion
- No genotype

FIGURE S6

A



Pearson coefficient is only 0.39 between NSC714184 (SOS thiophene (NSC 652287) and Nutlin

Pearson between TP53 WT status and Nutlin is highly significant whereas it is not significant for NSC714184 (SOS thiophene (NSC 652287) = 0.154

B

| Gene     | Correl. | Location | microRNA        | Correl. | Location | NSC    | Drug Name         | Correl. | Status       |
|----------|---------|----------|-----------------|---------|----------|--------|-------------------|---------|--------------|
| C6orf138 | 0.62    | 6p12.3   | hsa-miR-34a     | 0.56    | 1p36.22  | 756876 | nutlin-3          | 0.85    | Not Approved |
| FDXR     | 0.60    | 17q25.2  | hsa-miR-34a*    | 0.42    | 1p36.22  | 689874 | -                 | 0.55    | Not Approved |
| MDM2     | 0.59    | 12q15    | hsa-miR-34b*    | 0.39    | 11q23.1  | 689873 | -                 | 0.53    | Not Approved |
| CDKN1A   | 0.58    | 6p21.31  | hsa-miR-150*    | 0.39    | 19q13.32 | 689872 | -                 | 0.53    | Not Approved |
| TM4SF18  | 0.55    | 3q24     | hsa-miR-139-3p  | 0.32    | 11q13.4  | 125066 | Bleomycin         | 0.45    | FDA Approved |
| GDF15    | 0.55    | 19p13.11 | hsa-miR-330-3p  | 0.32    | 19q13.2  | 6171   | 1,8-cineole       | 0.45    | Not Approved |
| BAX      | 0.54    | 19q13.31 | hsa-miR-135a*   | 0.32    | 3p21.1   | 619003 | MX2               | 0.38    | Not Approved |
| RPS27L   | 0.52    | 15q22.31 | hsa-miR-501-5p  | 0.30    | Xp11.22  | 153353 | L-Alanosine       | 0.38    | Not Approved |
| RRM2B    | 0.52    | 8q22.3   | hsa-miR-874     | 0.30    | 5q31.2   | 26980  | Mitomycin         | 0.38    | FDA Approved |
| TMEM5    | 0.51    | 12q14.3  | hsa-miR-1226*   | 0.28    | 3p21.31  | 61586  | Phleomycin        | 0.38    | Not Approved |
| SPATA18  | 0.51    | 4q12     | hsa-miR-513a-5p | 0.28    | Xq27.3   | 145668 | Cyclocytidine HCl | 0.37    | Not Approved |
| XPC      | 0.51    | 3p25.1   | hsa-miR-629*    | 0.27    | 15q23    | 686288 | Aminoflavone      | 0.37    | Not Approved |
| DDB2     | 0.49    | 11p11.2  | hsa-miR-134     | 0.26    | 14q32.31 | 63878  | Cytarabine HCl    | 0.36    | FDA Approved |
| -----    |         |          |                 |         |          |        |                   |         |              |
| AMIGO3   | -0.49   | 3p21.31  | hsa-miR-15a     | -0.34   | 13q14.3  | 625457 | -                 | -0.42   | Not Approved |
| ZNF470   | -0.49   | 19q13.33 | hsa-miR-16-2*   | -0.34   | 3q25.33  | 651925 | -                 | -0.43   | Not Approved |
| LZIC     | -0.49   | 1p36.22  | hsa-miR-33a     | -0.38   | 22q13.2  | 655620 | -                 | -0.44   | Not Approved |
| USP1     | -0.50   | 1p31.3   | hsa-miR-130b    | -0.42   | 22q11.23 | 699807 | -                 | -0.44   | Not Approved |
| ZNF20    | -0.50   | 19p13.2  | hsa-miR-16      | -0.42   | 3q25.33  | 84423  | -                 | -0.45   | Not Approved |
| ZNF266   | -0.55   | 19p13.2  | hsa-miR-361-5p  | -0.43   | Xq21.2   | 726311 | -                 | -0.46   | Not Approved |
| ZNF44    | -0.58   | 19p13.2  | hsa-miR-15b     | -0.43   | 3q25.33  | 645647 | benzamide         | -0.48   | Not Approved |

Positive

Negative

FIGURE S7

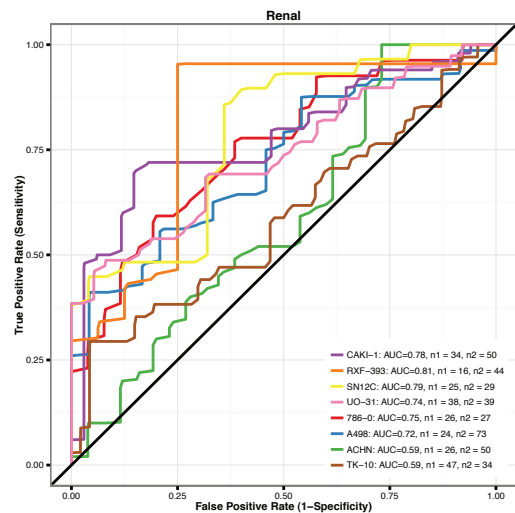
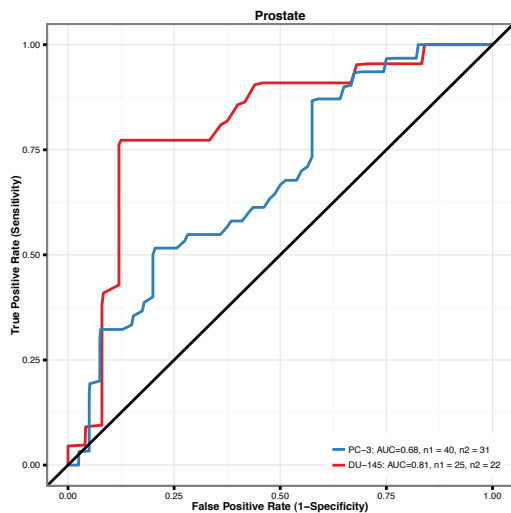
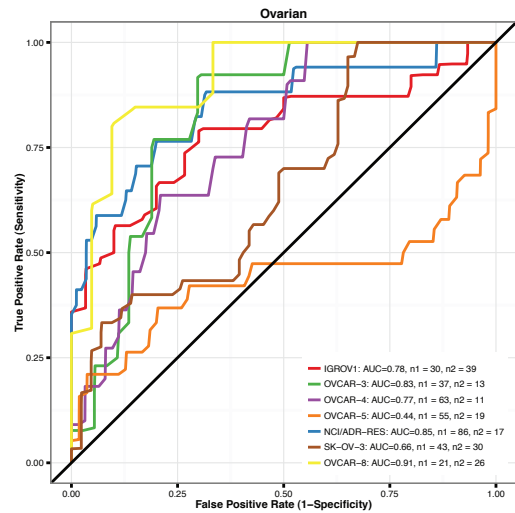
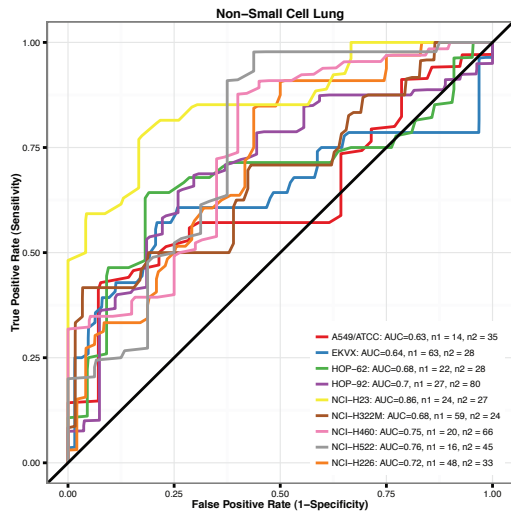
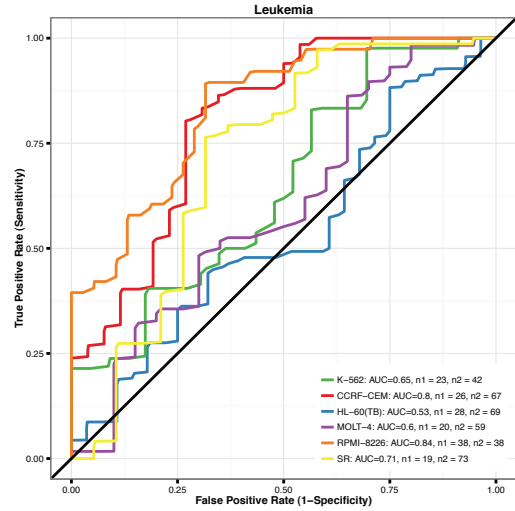
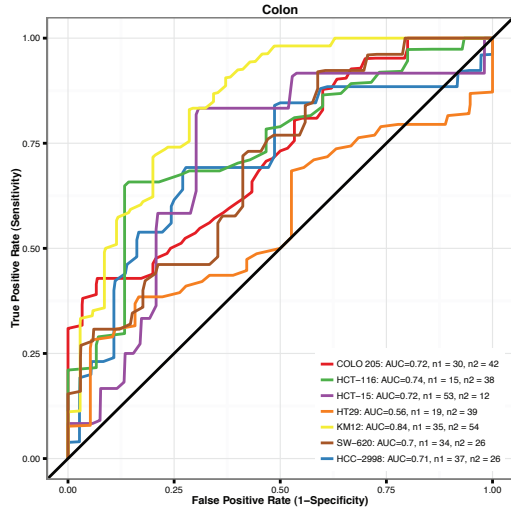
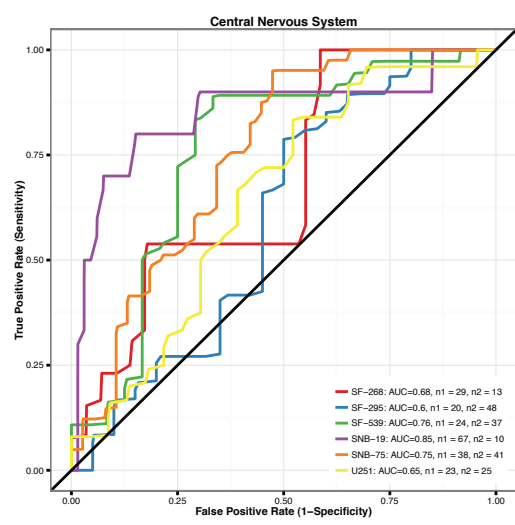
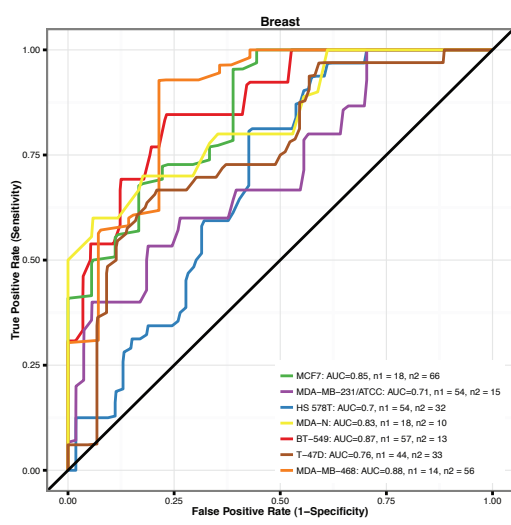


FIGURE S8