

Supplementary Material

| Number of Genes (Panel mean length) | Threshold mut/Mb | Pearson | Pearson High TMB | Pearson Low TMB | PPV | TPV | TNR | NPV | TP | FP | TN | FN |
|--|---------------------|---------|---------------------|--------------------|------|------|------|------|-------|------|-------|-------|
| 50 (0.27) | 5 | 0.94 | 0.93 | 0.17 | 0.83 | 0.47 | 0.91 | 0.70 | 11.9 | 2.9 | 31.3 | 13.1 |
| | 10 | | 0.90 | 0.25 | 0.94 | 0.69 | 0.98 | 0.96 | 11.1 | 0.78 | 45.2 | 1.93 |
| | 20 | | 0.90 | 0.31 | 0.95 | 0.79 | 0.96 | 0.95 | 9.4 | 0.5 | 46.5 | 2.5 |
| | 25.29 | | 0.89 | 0.36 | 0.93 | 0.87 | 0.98 | 0.97 | 9.5 | 0.8 | 47.1 | 1.4 |
| | 34.66 | | 0.89 | 0.56 | 0.88 | 0.84 | 0.97 | 0.97 | 8.4 | 1.2 | 47.8 | 1.5 |
| 100(0.55) | 5 | 0.97 | 0.96 | 0.24 | 0.86 | 0.52 | 0.93 | 0.73 | 13.04 | 2.2 | 31.78 | 11.96 |
| | 10 | | 0.95 | 0.34 | 0.97 | 0.92 | 0.99 | 0.98 | 11.91 | 0.39 | 45.61 | 1.09 |
| | 20 | | 0.94 | 0.42 | 0.98 | 0.88 | 0.97 | 0.97 | 10.63 | 0.23 | 46.77 | 1.37 |
| | 25.29 | | 0.94 | 0.49 | 0.95 | 0.85 | 0.99 | 0.99 | 10.49 | 0.64 | 47.36 | 0.5 |
| | 34.66 | | 0.94 | 0.69 | 0.91 | 0.92 | 0.98 | 0.98 | 9.2 | 1.01 | 47.99 | 0.78 |
| 200(1.09) | 5 | 0.98 | 0.98 | 0.33 | 0.88 | 0.56 | 0.94 | 0.75 | 14.1 | 2.1 | 31.9 | 10.9 |
| | 10 | | 0.97 | 0.45 | 0.98 | 0.96 | 0.99 | 0.99 | 12.53 | 0.2 | 45.78 | 0.5 |
| | 20 | | 0.97 | 0.54 | 0.99 | 0.94 | 1 | 0.98 | 11.27 | 0.07 | 46.93 | 0.73 |
| | 25.29 | | 0.97 | 0.62 | 0.96 | 0.99 | 0.99 | 1 | 10.88 | 0.52 | 47.48 | 0.12 |
| | 34.66 | | 0.97 | 0.80 | 0.93 | 0.96 | 0.98 | 0.99 | 9.61 | 0.73 | 48.27 | 0.39 |
| 300(1.64) | 5 | 0.99 | 0.99 | 0.39 | 0.88 | 0.59 | 0.94 | 0.76 | 4.85 | 2.08 | 31.92 | 10.15 |
| | 10 | | 0.98 | 0.53 | 0.99 | 0.98 | 0.99 | 0.99 | 12.79 | 0.18 | 45.81 | 0.2 |
| | 20 | | 0.98 | 0.62 | 1 | 0.95 | 1 | 0.99 | 11.44 | 0.02 | 46.98 | 0.56 |
| | 25.29 | | 0.98 | 0.69 | 0.96 | 0.99 | 0.99 | 1 | 10.94 | 0.49 | 47.51 | 0.06 |
| | 34.66 | | 0.98 | 0.86 | 0.95 | 0.97 | 0.99 | 0.99 | 9.74 | 0.57 | 48.43 | 0.25 |

Table S1. Table of correlation between WES TMB and TMB computed using random mutated genes panels of different sizes. For each group of panels, we have calculated the mean of correlation, PPV, TPR, TNR and NPV. The analysis have been performed for each threshold considered in the paper.

| Number of Genes (Panel mean length) | Threshold mut/Mb | Pearson | Pearson High TMB | Pearson Low TMB | PPV | TPR | TNR | NPV | TP | FP | TN | FN |
|--|---------------------|---------|---------------------|--------------------|------|------|------|------|----|----|----|----|
| 500 (6.44) | 5 | 0.99 | 0.99 | 0.77 | 0.95 | 0.76 | 0.97 | 0.85 | 19 | 1 | 33 | 6 |
| | 10 | | 0.98 | 0.89 | 1 | 1 | 1 | 1 | 13 | 0 | 46 | 0 |
| | 20 | | 0.98 | 0.93 | 1 | 1 | 1 | 1 | 12 | 0 | 47 | 0 |
| | 25.29 | | 0.98 | 0.95 | 0.92 | 1 | 0.98 | 1 | 11 | 1 | 47 | 0 |
| | 34.66 | | 0.98 | 0.97 | 1 | 1 | 1 | 1 | 10 | 0 | 49 | 0 |
| 409 (5.49) | 5 | 0.99 | 0.99 | 0.74 | 0.91 | 0.8 | 0.94 | 0.86 | 20 | 2 | 32 | 5 |
| | 10 | | 0.98 | 0.88 | 1 | 1 | 1 | 1 | 13 | 0 | 46 | 0 |
| | 20 | | 0.98 | 0.92 | 1 | 1 | 1 | 1 | 12 | 0 | 47 | 0 |
| | 25.29 | | 0.98 | 0.94 | 0.92 | 1 | 0.98 | 1 | 11 | 1 | 47 | 0 |
| | 34.66 | | 0.98 | 0.96 | 1 | 1 | 1 | 1 | 10 | 0 | 49 | 0 |
| 300 (4.28) | 5 | 0.99 | 0.98 | 0.70 | 0.91 | 0.80 | 0.94 | 0.86 | 20 | 2 | 32 | 5 |
| | 10 | | 0.98 | 0.85 | 1 | 1 | 1 | 1 | 13 | 0 | 46 | 0 |
| | 20 | | 0.98 | 0.90 | 1 | 1 | 1 | 1 | 12 | 0 | 47 | 0 |
| | 25.29 | | 0.98 | 0.93 | 0.92 | 1 | 0.98 | 1 | 11 | 1 | 47 | 0 |
| | 34.66 | | 0.98 | 0.96 | 0.91 | 1 | 0.98 | 1 | 10 | 1 | 48 | 0 |
| 200 (3.05) | 5 | 0.98 | 0.98 | 0.65 | 0.86 | 0.76 | 0.91 | 0.84 | 19 | 3 | 31 | 6 |
| | 10 | | 0.97 | 0.82 | 1 | 1 | 1 | 1 | 12 | 0 | 47 | 0 |
| | 20 | | 0.97 | 0.88 | 1 | 1 | 1 | 1 | 12 | 0 | 47 | 0 |
| | 25.29 | | 0.97 | 0.91 | 0.92 | 1 | 0.98 | 1 | 11 | 1 | 47 | 0 |
| | 34.66 | | 0.97 | 0.94 | 0.91 | 1 | 0.98 | 1 | 10 | 1 | 48 | 0 |
| 100 (1.8) | 5 | 0.98 | 0.97 | 0.60 | 0.87 | 0.80 | 0.91 | 0.86 | 20 | 3 | 31 | 5 |
| | 10 | | 0.97 | 0.79 | 1 | 1 | 1 | 1 | 13 | 0 | 46 | 0 |
| | 20 | | 0.97 | 0.86 | 1 | 1 | 1 | 1 | 12 | 0 | 47 | 0 |
| | 25.29 | | 0.97 | 0.89 | 0.92 | 1 | 0.98 | 1 | 11 | 1 | 47 | 0 |
| | 34.6 | | 0.96 | 0.92 | 0.91 | 1 | 0.98 | 1 | 10 | 1 | 48 | 0 |
| 50 (1.08) | 5 | 0.97 | 0.96 | 0.55 | 1 | 0.76 | 1 | 0.85 | 19 | 0 | 34 | 6 |
| | 10 | | 0.95 | 0.73 | 1 | 1 | 1 | 1 | 13 | 0 | 46 | 0 |
| | 20 | | 0.95 | 0.81 | 1 | 1 | 1 | 1 | 12 | 0 | 47 | 0 |
| | 25.29 | | 0.95 | 0.86 | 0.92 | 1 | 0.98 | 1 | 11 | 1 | 47 | 0 |
| | 34.66 | | 0.95 | 0.88 | 0.91 | 1 | 0.98 | 1 | 10 | 1 | 48 | 0 |

Table S2. Most Frequently mutated genes panels correlation. Patients number: Threshold 5 mut/Mb 126 H-TMB, 172 L-TMB; Threshold 10 mut/Mb 66 H-TMB, 232 L-TMB; Threshold 20 mut/Mb 60 H-TMB, 238 L-TMB; Threshold 25.29 mut/Mb 58 H-TMB, 240 L-TMB; Threshold 34.66 mut/Mb 51 H-TMB, 247 L-TMB. PPV, TPR, TNR and NPV of all colon cancer thresholds have been calculated with logistic regression for all panels with the most mutated genes.

| Threshold mut/Mb | Pearson | Pearson High TMB | Pearson Low TMB | PPV | TPR | TNR | NPV | TP | FP | TN | FN |
|------------------|---------|------------------|-----------------|------|------|------|------|----|----|----|----|
| 4.46 | 0.93 | 0.92 | 0.40 | 0.86 | 0.62 | 0.90 | 0.70 | 18 | 3 | 26 | 11 |
| 5 | | 0.92 | 0.42 | 0.87 | 0.52 | 0.94 | 0.73 | 13 | 2 | 32 | 12 |
| 10 | | 0.89 | 0.41 | 0.93 | 1 | 0.98 | 1 | 13 | 1 | 45 | 0 |
| 20 | | 0.88 | 0.56 | 1 | 1 | 1 | 1 | 12 | 0 | 47 | 0 |
| 20.34 | | 0.88 | 0.56 | 1 | 1 | 1 | 1 | 12 | 0 | 47 | 0 |
| 25.29 | | 0.87 | 0.62 | 0.91 | 0.91 | 0.98 | 0.98 | 10 | 1 | 47 | 1 |
| 34.66 | | 0.86 | 0.75 | 0.90 | 0.90 | 0.98 | 0.98 | 9 | 1 | 48 | 1 |

Table S3. Correlation between WES and AmpliSeq for Illumina Comprehensive Cancer Panel. PPV, TPR, TNR and NPV of all colon cancer thresholds have been calculated with logistic regression for AmpliSeq for Illumina Comprehensive Cancer Panel

| | Pearson | Pearson H-TMB | Pearson L-TMB | PPV | TPR | TNR | NPV | TP | FP | TN | FN |
|-----------------|---------|---------------|---------------|------|------|------|------|----|----|----|----|
| UCEC-UCS | 0.98 | 0.98 | 0.77 | 1.00 | 0.93 | 1 | 0.95 | 42 | 0 | 62 | 3 |
| STAD | 0.97 | 0.97 | 0.79 | 0.88 | 0.94 | 0.97 | 0.98 | 15 | 2 | 64 | 1 |
| COAD | 0.97 | 0.96 | 0.74 | 1 | 0.83 | 1 | 0.96 | 10 | 0 | 46 | 2 |
| SKCM | 0.98 | 0.98 | 0.86 | 0.90 | 0.88 | 0.88 | 0.86 | 45 | 5 | 36 | 6 |
| BLCA | 0.93 | 0.95 | 0.74 | 1.00 | 0.78 | 1 | 0.97 | 7 | 0 | 72 | 2 |
| CESC | 0.99 | 0.99 | 0.70 | 0.87 | 0.87 | 0.98 | 0.98 | 7 | 1 | 50 | 1 |
| LUSC | 0.91 | 0.89 | 0.78 | 0.94 | 0.72 | 0.99 | 0.92 | 16 | 1 | 75 | 6 |
| LUAD | 0.95 | 0.90 | 0.89 | 0.74 | 0.83 | 0.91 | 0.94 | 20 | 7 | 70 | 4 |
| LIHC | 0.90 | 0.83 | 0.79 | 1.00 | 0.50 | 1 | 0.99 | 1 | 0 | 77 | 1 |
| THCA | 1 | 1 | 0.87 | 1.00 | 0.50 | 1 | 0.99 | 1 | 0 | 96 | 1 |
| OV | 0.92 | 0.88 | 0.80 | 0.62 | 0.71 | 0.92 | 0.94 | 5 | 3 | 33 | 2 |
| ESCA | 0.84 | 0.86 | 0.79 | 0.50 | 0.75 | 0.91 | 0.97 | 3 | 3 | 29 | 1 |
| PRAD | 0.99 | 1 | 0.55 | NA | 0 | 1 | 0.99 | 0 | 0 | 97 | 1 |
| PAAD | 1 | 1 | 0.65 | 1 | 1 | 1 | 1 | 1 | 0 | 33 | 0 |
| KIRC | 0.98 | 1 | 0.60 | 1 | 1 | 1 | 1 | 1 | 0 | 66 | 0 |
| KIRP | 0.83 | 0.98 | 0.74 | 0 | 0 | 0.96 | 0.98 | 0 | 2 | 54 | 1 |
| ACC | 0.94 | 0.93 | 0.81 | NA | 0 | 1 | 0.98 | 0 | 0 | 43 | 1 |

Table S4. Correlation, Precision, and Recall of each TCGA tumor between TMB analyzed with the panel built with the 44 most mutated genes and WES TMB using threshold 20 mut/Mb. The table also reports the True Negative Rate, Negative Predicted Value, and the confusion matrix for each cancer type.

1 SUPPLEMENTARY DATA

In Table. S3, we describe the results of the AmpliSeq for Illumina Comprehensive Cancer Panel. The correlation is very high without splitting the patients into H-TMB and L-TMB groups. However, while it stays stable for the H-TMB patients, the correlation strongly decreases for the L-TMB one. The comprehensive panel properly partitions the patients into High and Low TMB using logistic regression, showing high sensitivity and specificity. Therefore, such a panel could suit TMB computation in the clinical setting.

In what follows, we report the statistical analysis of each tumor.

| | Threshold | Pearson | Pearson H-TMB | Pearson L-TMB | PPV | TPR | TNR | NPV | TP | FP | TN | FN |
|------------|-----------|---------|---------------|---------------|------|------|------|------|----|----|----|----|
| TCGA 126 | 5 | 0.96 | 0.94 | 0.57 | 1 | 0.6 | 1 | 0.90 | 3 | 0 | 19 | 2 |
| | 10 | | 0.92 | 0.67 | 1 | 1 | 1 | 1 | 3 | 0 | 21 | 0 |
| | 20 | | 0.91 | 0.77 | 0.75 | 1 | 0.95 | 1 | 3 | 1 | 20 | 0 |
| | 25.29 | | 0.91 | 0.83 | 1 | 1 | 1 | 1 | 3 | 0 | 22 | 0 |
| | 34.66 | | 0.89 | 0.94 | 1 | 1 | 1 | 1 | 2 | 0 | 23 | 0 |
| Genentech | 5 | 0.95 | 0.96 | 0.51 | 1 | 1 | 1 | 1 | 3 | 0 | 10 | 0 |
| | 10 | | 0.96 | 0.55 | 1 | 1 | 1 | 1 | 3 | 0 | 11 | 0 |
| | 20 | | 0.97 | 0.92 | 1 | 1 | 1 | 1 | 2 | 0 | 11 | 0 |
| | 25.29 | | 0.97 | 0.92 | NA | 0 | 1 | 0.92 | 0 | 0 | 12 | 1 |
| | 34.66 | | 0.99 | 0.95 | NA | NA | 1 | 1 | 0 | 0 | 13 | 0 |
| COCA | 5 | 0.97 | 0.97 | 0.65 | 0.84 | 0.67 | 0.91 | 0.79 | 2 | 0 | 23 | 0 |
| | 10 | | 0.97 | 0.50 | 0.83 | 0.67 | 0.95 | 0.89 | 2 | 0 | 23 | 0 |
| | 20 | | 0.97 | 0.64 | 1 | 0.50 | 1 | 0.92 | 4 | 0 | 50 | 4 |
| | 25.29 | | 0.97 | 0.62 | 0.83 | 0.83 | 0.98 | 0.98 | 5 | 1 | 51 | 1 |
| | 34.66 | | 0.97 | 0.72 | 1 | 0.6 | 1 | 0.96 | 3 | 0 | 53 | 2 |
| Colonomics | 5 | 0.72 | 0.35 | 0.47 | 1 | 0.33 | 1 | 0.71 | 1 | 0 | 5 | 2 |
| | 10 | | NA | 0.72 | 1 | 1 | NA | NA | NA | NA | NA | NA |
| | 20 | | NA | 0.72 | NA | NA | NA | NA | NA | NA | 8 | NA |
| | 25.29 | | NA | 0.72 | 1 | 1 | NA | NA | NA | NA | NA | NA |
| | 34.66 | | NA | 0.72 | 1 | 1 | NA | NA | NA | NA | 8 | NA |
| Li-Jp | 20 | 0.99 | 0.99 | 0.53 | 0.93 | 0.83 | 0.84 | 0.67 | 40 | 3 | 16 | 8 |
| dbGap* | 10 | 0.77 | 1 | 0.79 | NA | 0 | 1 | 0.95 | 0 | 0 | 18 | 1 |

Table S5. Correlation between WES TMB and 44 genes panel TMB using all colon cancer thresholds. PPV, TPR, TNR and NPV for the six datasets have been calculated through logistic regression. All the colon thresholds have been used for Genentech, Colonomics, TCGA 126, and COCA. For Liver, we used only threshold 20 mut/Mb and threshold 10 mut/Mb for dbGaP. The table also reports the True Negative Rate, Negative Predicted Value, and the confusion matrix for each cancer type.

| Ten most frequently mutated genes | #mutation in all patients | Patients with the mutations | Mean mutations per patient (SD) | Patients with mutations and high TMB level (Out of 60) | Patients with mutations and low TMB level (Out of 238) | Mutations in H-TMB patients - Mean of mutations per high patient (SD) | Mutations in L-TMB patients - Mean mutations per low patient (SD) | Expected Mutation rate | Observed Mutation rate H-TMB | Observed Mutation rate L-TMB |
|-----------------------------------|---------------------------|-----------------------------|---------------------------------|--|--|---|---|------------------------|------------------------------|------------------------------|
| TTN | 369 | 117 (39%) | 3.15 (5.1) | 55 (92%) | 62 (26%) | 298 (6.8) | 71 (1.14 (0.4)) | 0.010 | 0.042*** | 0.002*** |
| SYNE1 | 301 | 109 (36%) | 2.76 (3.5) | 55 (92%) | 54 (23%) | 236 (4.4) | 65 (1.20 (0.5)) | 0.022 | 0.084*** | 0.005*** |
| MUC19 | 214 | 91 (30%) | 2.35 (2.7) | 45 (75%) | 46 (19%) | 160 (3.4) | 54 (1.17 (0.5)) | 0.024 | 0.090*** | 0.008*** |
| RYR2 | 209 | 92 (31%) | 2.27 (2.9) | 53 (88%) | 39 (16%) | 166 (3.6) | 43 (1.10 (0.3)) | 0.039 | 0.155*** | 0.010*** |
| NEB | 192 | 68 (23%) | 2.82 (3.1) | 46 (77%) | 22 (9%) | 166 (3.6) | 26 (1.18 (0.4)) | 0.021 | 0.090*** | 0.004*** |
| LRP1B | 169 | 88 (29%) | 1.92 (1.9) | 45 (75%) | 43 (18%) | 121 (2.4) | 48 (1.12 (0.3)) | 0.035 | 0.123*** | 0.012*** |
| MUC16 | 168 | 75 (25%) | 2.24 (2.9) | 42 (70%) | 33 (14%) | 132 (3.7) | 36 (1.09 (0.3)) | 0.013 | 0.050*** | 0.003*** |
| DYNC2H1 | 152 | 83 (28%) | 1.83 (1.6) | 52 (87%) | 31 (13%) | 119 (1.9) | 33 (1.06 (0.2)) | 0.034 | 0.132*** | 0.009*** |
| RYR3 | 143 | 64 (21%) | 2.23 (2.8) | 40 (67%) | 24 (10%) | 116 (3.4) | 27 (1.12 (0.4)) | 0.024 | 0.095*** | 0.006*** |
| COL11A1 | 141 | 74 (25%) | 1.90 (2.2) | 35 (58%) | 39 (16%) | 99 (3) | 42 (1.08 (0.3)) | 0.052 | 0.181*** | 0.019** |

Table S6. Ten most frequently genes percentage, mean, standard deviation, and expected and observed mutation rate in Colon adenocarcinoma with threshold 20. The statistical significance: ***p-val < 0.001, **p-val < 0.01. The analysis clearly show that the mutation rate within the H-TMB class is much higher and the expected one. Conversely, the mutation rate within the L-TMB class is lower than the expected.

| Ten most frequently mutated genes | Patients with mutations and H-TMB level (Out of 126) | Mutations in high TMB patients - Mean of mutations per high patient (SD) | | Patients with mutations and low TMB level (Out of 172) | Mutations in low TMB patients - Mean of mutations per low patient (SD) | |
|-----------------------------------|--|--|----------------|--|--|----------------|
| TTN | 82 (65%) | 328 | 4 (5.9) | 35 (20%) | 41 | 1.17 (0.38) |
| SYNE1 | 74 (59%) | 263 | 3.55 (4) | 35 (20%) | 38 | 1.08 (0.28) |
| MUC19 | 63 (50%) | 180 | 2.86 (3.1) | 28 (16%) | 34 | 1.21 (0.56) |
| RYR2 | 70 (55%) | 185 | 2.64 (3.3) | 22 (13%) | 24 | 1.09 (0.93) |
| NEB | 55 (44%) | 177 | 3.21 (3.4) | 13 (7%) | 15 | 1.15 (0.37) |
| LRP1B | 63 (50%) | 142 | 2.25 (2.2) | 25 (14%) | 27 | 1.08 (0.28) |
| MUC16 | 59 (47%) | 152 | 2.58 (3.2) | 16 (9%) | 16 | 1 (0) |
| DYNC2H1 | 67 (53%) | 134 | 2 (1.7) | 16 (9%) | 18 | 1.12 (0.35) |
| RYR3 | 52 (41%) | 131 | 2.52 (3.05) | 12 (7%) | 12 | 1 (0) |
| COL11A1 | 51 (40%) | 118 | 2.31 (2.6) | 23 (13%) | 23 | 1 (0) |

Table S7. Ten most frequently genes percentage, mean, standard deviation, fisher and welch test in Colon adenocarcinoma with threshold 5 mut/Mb

| Ten most frequently mutated genes | Patients with mutations and high TMB level (Out of 66) | Mutations in high TMB patients - Mean of mutations per high patient (SD) | Patients with mutations and low TMB level (Out of 232) | Mutations in low TMB patients - Mean of mutations per low patient (SD) |
|-----------------------------------|--|--|--|--|
| TTN | 58 (89%) | 301 5.19 (6.7) | 59 (25%) | 68 1.15 (0.4) |
| SYNE1 | 57 (86%) | 240 4.21 (4.4) | 59 (25%) | 61 1.03 (0.5) |
| MUC19 | 48 (73%) | 164 3.42 (3.4) | 43 (18%) | 50 1.16 (0.5) |
| RYR2 | 56 (85%) | 169 3.02 (3.6) | 36 (18%) | 40 1.11 (0.3) |
| NEB | 46 (70%) | 166 3.61 (3.6) | 22 (9%) | 26 1.18 (0.4) |
| LRP1B | 49 (74%) | 125 2.55 (2.4) | 39 (17%) | 44 1.13 (0.3) |
| MUC16 | 45 (68%) | 135 3 (3.6) | 30 (13%) | 33 1.1 (0.3) |
| DYNC2H1 | 54 (82%) | 121 2.24 (1.9) | 29 (12%) | 31 1.06 (0.3) |
| RYR3 | 41 (62%) | 117 2.85 (3.3) | 23 (10%) | 26 1.13 (0.4) |
| COL11A1 | 40 (61%) | 104 2.60 (2.9) | 34 (15%) | 37 1.09 (0.3) |

Table S8. Ten most frequently genes percentage, mean, standard deviation, Fisher and Welch test in Colon adenocarcinoma with threshold 10 mut/Mb

| Ten most frequently mutated genes | Patients with mutations and high TMB level (Out of 58) | Mutations in high TMB patients - Mean of mutations per high patient (SD) | Patients with mutations and low TMB level (Out of 240) | Mutations in low TMB patients - Mean of mutations per low patient (SD) |
|-----------------------------------|--|--|--|--|
| TTN | 53 (91%) | 293 5.53 (6.9) | 64 (27%) | 76 1.19 (0.4) |
| SYNE1 | 54 (93%) | 235 4.35 (4.5) | 55 (23%) | 66 1.20 (0.5) |
| MUC19 | 44 (76%) | 158 3.59 (3.5) | 47 (19%) | 56 1.19 (0.5) |
| RYR2 | 51 (88%) | 164 3.21 (3.7) | 41 (17%) | 45 1.10 (0.3) |
| NEB | 46 (79%) | 166 3.61 (3.6) | 22 (9%) | 26 1.18 (0.4) |
| LRP1B | 45 (75%) | 121 2.69 (2.4) | 43 (18%) | 48 1.17 (0.3) |
| MUC16 | 41 (71%) | 131 3.19 (3.7) | 34 (14%) | 37 1.09 (0.3) |
| DYNC2H1 | 51 (88%) | 118 2.31 (1.9) | 32 (13%) | 34 1.06 (0.2) |
| RYR3 | 39 (67%) | 115 2.95 (3.4) | 25 (10%) | 28 1.12 (0.4) |
| COL11A1 | 33 (57%) | 96 2.90 (3.1) | 41 (17%) | 45 1.10 (0.3) |

Table S9. Ten most frequently genes percentage, mean, standard deviation, Fisher and Welch test in Colon adenocarcinoma with threshold 25.29 mut/Mb

| Ten most frequently mutated genes | Patients with mutations and high TMB level (Out of 51) | Mutations in high TMB patients - Mean of mutations per high patient (SD) | Patients with mutations and low TMB level (Out of 247) | Mutations in low TMB patients - Mean of mutations per low patient (SD) |
|-----------------------------------|--|--|--|--|
| TTN | 49 (96%) | 283 5.77 (7.1) | 68 (27%) | 86 1.26 (0.7) |
| SYNE1 | 49 (96%) | 228 4.65 (4.6) | 60 (24%) | 73 1.22 (0.5) |
| MUC19 | 40 (78%) | 153 3.82 (3.6) | 51 (21%) | 61 1.20 (0.5) |
| RYR2 | 46 (90%) | 156 3.39 (3.8) | 46 (19%) | 53 1.15 (0.4) |
| NEB | 44 (86%) | 164 3.73 (3.6) | 24 (10%) | 28 1.17 (0.4) |
| LRP1B | 41 (80%) | 115 2.80 (2.5) | 47 (19%) | 54 1.15 (0.7) |
| MUC16 | 39 (76%) | 129 3.31 (3.8) | 36 (14%) | 39 1.08 (0.3) |
| DYNC2H1 | 46 (90%) | 111 2.41 (2) | 37 (15%) | 41 1.11 (0.3) |
| RYR3 | 37 (72%) | 112 3.03 (3.5) | 27 (11%) | 31 1.15 (0.4) |
| COL11A1 | 31 (61%) | 94 3.03 (3.2) | 43 (17%) | 47 1.09 (0.3) |

Table S10. Ten most frequently genes percentage, mean, standard deviation, Fisher and Welch test in Colon adenocarcinoma with threshold 34.66 mut/Mb

| Tumor | Genes |
|-----------------|---|
| COAD | TTN – SYNE1 – MUC19 – RYR2 – NEB – LRP1B – MUC16 – DYNC2H1 – RYR3 – COL11A1 |
| ESCA | TTN – MUC19 – LRP1B – CSMD3 – SNHG14 – SYNE1 – MUC16 – RYR2 – HMCN1 – COL11A1 |
| STAD | TTN – SYNE1 – LRP1B – SNHG14 – CSMD3 – MYHAS – HMCN1 – MUC16 – DNAH5 – SPTA1 |
| LIHC | ALB – TTN – CSMD3 – RYR2 – MUC19 – OBSCN – HMCN1 – COL11A1 – MUC16 – LRP1B |
| PAAD | TTN – SYNE1 – MUC16 – HMCN1 – LRP1B – SNHG14 – MACF1 – RYR3 – USH2A – NEB |
| BLCA | TTN – SNHG14 – SYNE1 – CSMD3 – HMCN1 – MYHAS – MUC16 – RYR2 – LRP1B – SYNE2 |
| KIRP | TTN – LRP2 – SYNE1 – CUBN – SYNE2 – UBR4 – NEB – PKHD1 – OBSCN – DST |
| KIRC | TTN – PBRM1 – LRP2 – NEB – RNR2 – COL11A1 – HMCN1 – VHL – SYNE1 – SYNE2 |
| ACC | NF1 – MUC16 – TTN – MUC19 – RYR1 – LRP1 – CSMD1 – ABCA13 – HMCN1 – LRP1B |
| UCEC-UCS | TTN – NEB – RYR2 – DMD – SYNE1 – MUC16 – CSMD3 – LRP1B – HMCN1 – DST |
| CESC | TTN – DMD – MUC16 – RYR2 – NEB – MUC19 – SNHG14 – CSMD3 – OBSCN – SYNE1 |
| OV | TTN – MUC16 – SYNE1 – CSMD3 – MYHAS – LRP2 – UBR4 – RYR2 – PKHD1 – DST |
| PRAD | SYNE1 – TTN – LRP1B – SNHG14 – MUC16 – CSMD3 – HMCN1 – MYHAS – KMT2D – WASL |
| SKCM | TTN – MUC16 – SNHG14 – MYHAS – DNAH5 – MGAM – LRP1B – CSMD2 – DNAH9 – RYR1 |
| THCA | TTN – SYNE1 – HMCN1 – MACF1 – KIAA1109 – TG – MUC16 – SNHG14 – UTP20 – MYHAS |
| LUSC | TTN – SNHG14 – CSMD3 – LRP1B – SYNE1 – MUC16 – RYR2 – USH2A – COL22A1 – SPTA1 |
| LUAD | TTN – LRP1B – CSMD3 – SNHG14 – RYR2 – MUC16 – USH2A – SPTA1 – MYHAS – COL11A1 |

Table S11. Ten most frequently mutated genes in all cancer types analyzed

| Ten most frequently mutated genes | #Mutation in all patients | Patients with the mutations (Out of 302) | Mean of mutations per patient (SD) | Patients with mutations and H-TMB level (Out of 43) | Mutations in H-TMB patients - Mean of mutations per high patient (SD) | Patients with mutations and L-TMB level (Out of 259) | Mutations in L-TMB patients - Mean of mutations per low patient (SD) |
|-----------------------------------|---------------------------|--|------------------------------------|---|---|--|--|
| TTN | 208 | 90 (30%) | 2,31 (5.6) | 33 (77%) | 145 4,39 (9) | 57 (22%) | 63 1,1 (0,3) |
| DMD | 116 | 82 (27%) | 1,41 (1.2) | 29 (67%) | 58 2 (1.8) | 53 (20%) | 58 1,09 (0.3) |
| MUC16 | 114 | 67 (22%) | 1,70 (1.5) | 27 (63%) | 63 2,33 (2.1) | 40 (15%) | 51 1,27 (0.7) |
| RYR2 | 103 | 60 (20%) | 1,72 (3) | 26 (60%) | 63 2,42 (4.5) | 34 (13%) | 40 1,18 (0.4) |
| NEB | 101 | 62 (20%) | 1,63 (1.8) | 26 (60%) | 60 2,31 (2.7) | 36 (14%) | 41 1,14 (0.4) |
| MUC19 | 98 | 60 (20%) | 1,63 (1.8) | 28 (65%) | 60 2,14 (2.5) | 32 (12%) | 38 1,19 (0.5) |
| SNHG14 | 90 | 57 (19%) | 1,58 (1.9) | 20 (46%) | 51 2,55 (3) | 37 (14%) | 39 1,05 (0.7) |
| CSMD3 | 88 | 66 (22%) | 1,33 (0.9) | 23 (53%) | 42 1,83 (1.4) | 43 (17%) | 46 1,07 (0.3) |
| OBSCN | 88 | 47 (15%) | 1,87 (2) | 21 (49%) | 57 2,71 (2.7) | 26 (10%) | 31 1,19 (0.5) |
| SYNE1 | 88 | 51 (17%) | 1,72 (1.9) | 24 (56%) | 59 2,46 (2.6) | 27 (10%) | 29 1,07 (0.3) |

Table S12. Ten most frequently genes percentage, mean, standard deviation, fisher and welch test in Cervical squamous cell carcinoma and Endocervical adenocarcinoma with threshold 20 mut/Mb

| Ten most frequently mutated genes | #mutation in all patients | Patients with the mutations (Out of 180) | Mean of mutations per patient (SD) | Patients with mutations and H-TMB level (Out of 20) | Mutations in high TMB patients - Mean of mutations per high patient (SD) | Patients with mutations and low TMB level (Out of 160) | Mutations in low TMB patients - Mean of mutations per low patient (SD) |
|-----------------------------------|---------------------------|--|------------------------------------|---|--|--|--|
| TTN | 185 | 100 (55%) | 1.85 (1.1) | 19 (95%) | 52 2,74 (1.4) | 81 (51%) | 133 1,64 (0.9) |
| MUC19 | 131 | 74 (41%) | 1.77 (1) | 17 (85%) | 38 2,23 (1) | 57 (36%) | 93 1,63 (1) |
| LRP1B | 128 | 79 (44%) | 1.62 (1.1) | 14 (70%) | 32 2,28 (1.7) | 65 (41%) | 96 1,47 (0.9) |
| CSMD3 | 103 | 69 (38%) | 1,49 (1) | 12 (60%) | 28 2,33 (1.9) | 57 (36%) | 75 1,31 (0.5) |
| SNHG14 | 102 | 64 (35%) | 1,59 (1) | 15 (75%) | 35 2,33 (1.4) | 49 (31%) | 67 1,37 (0.7) |
| SYNE1 | 96 | 66 (37%) | 1.45 (0.8) | 15 (75%) | 33 2,2 (1.1) | 51 (32%) | 63 1,23 (0.5) |
| MUC16 | 85 | 63 (35%) | 1.35 (0.7) | 13 (65%) | 23 1,77 (1) | 50 (31%) | 62 1,24 (0.6) |
| RYR2 | 80 | 59 (33%) | 1.35 (0.6) | 15 (75%) | 25 1,67 (0.9) | 44 (27%) | 55 1,25 (0.5) |
| HMCN1 | 79 | 62 (34%) | 1,27 (0.6) | 12 (60%) | 18 1,5 (0.9) | 50 (31%) | 61 1,22 (0.5) |
| COL11A1 | 75 | 58 (32%) | 1.29 (0.6) | 9 (45%) | 16 1,78 (0.8) | 49 (31%) | 59 1,20 (0.4) |

Table S13. Ten most frequently genes percentage, mean, standard deviation, fisher and welch test in Esophageal carcinoma with threshold 20 mut/Mb

| Ten most frequently mutated genes | #mutation in all patients | Patients with the mutations | Mean of mutations per patient | Patients with mutations and high TMB level (Out of 38) | Number of mutations in high TMB patients - Mean of mutations per high patient (SD) | Patients with mutations and low TMB level (Out of 181) | Number of mutations in low TMB patients - Mean of mutations per low patient (SD) |
|-----------------------------------|---------------------------|-----------------------------|-------------------------------|--|--|--|--|
| TTN | 273 | 111 (51%) | 2.46 (1.9) | 35 (92%) | 132 3.77 (2.3) | 76 (42%) | 141 1.85 (1.3) |
| MUC16 | 166 | 96 (44%) | 1.73 (1) | 27 (71%) | 59 2.18 (1.2) | 69 (38%) | 107 1.55 (0.8) |
| SYNE1 | 95 | 64 (29%) | 1.48 (1) | 22 (58%) | 41 1.86 (1.3) | 42 (23%) | 54 1.28 (0.7) |
| CSMD3 | 84 | 64 (29%) | 1.31 (0.6) | 18 (47%) | 26 1.44 (0.6) | 46 (25%) | 58 1.26 (0.6) |
| MYHAS | 82 | 64 (29%) | 1.28 (0.6) | 23 (60%) | 38 1.65 (0.9) | 41 (23%) | 44 1.07 (0.3) |
| LRP2 | 79 | 63 (29%) | 1.25 (0.5) | 18 (47%) | 27 1.5 (0.7) | 45 (25%) | 52 1.15 (0.4) |
| UBR4 | 79 | 56 (25%) | 1.41 (0.9) | 20 (53%) | 31 1.55 (1.2) | 36 (20%) | 48 1.33 (0.6) |
| RYR2 | 76 | 63 (29%) | 1.21 (0.5) | 18 (47%) | 21 1.67 (0.4) | 45 (25%) | 55 1.22 (0.5) |
| PKHD1 | 74 | 61 (28%) | 1.21 (0.5) | 23 (60%) | 31 1.35 (0.6) | 38 (21%) | 43 1.13 (0.3) |
| DST | 73 | 54 (25%) | 1.35 (0.6) | 15 (39%) | 22 1.47 (0.8) | 39 (21%) | 51 1.31 (0.6) |

Table S14. Ten most frequently genes percentage, mean, standard deviation, fisher and welch test in Ovarian serous cystadenocarcinoma in threshold 20 mut/Mb

| Ten most frequently mutated genes | #mutation in all patients | Patients with the mutations (Out of 540) | Mean of mutations per patient (SD) | Patients with mutations and H-TMB level (Out of 227) | Number of mutations in high TMB patients - Mean of mutations per high patient (SD) | Patients with mutations and low TMB level (Out of 313) | Number of mutations in low TMB patients - Mean of mutations per low patient (SD) |
|-----------------------------------|---------------------------|--|------------------------------------|--|--|--|--|
| TTN | 2745 | 265 (49%) | 10.36 (17.2) | 197 (87%) | 2667 13.54 (18.9) | 68 (22%) | 78 1.15 (0.4) |
| NEB | 1503 | 217 (40%) | 6.93 (9.5) | 170 (75%) | 1445 8.5 (10.2) | 47 (15%) | 58 1.23 (0.5) |
| RYR2 | 1383 | 233 (43%) | 5.93 (8.6) | 175 (77%) | 1315 7.51 (9.4) | 58 (18%) | 68 1.17 (0.4) |
| DMD | 1374 | 216 (40%) | 6.36 (9) | 169 (74%) | 1321 7.82 (9.6) | 47 (15%) | 53 1.13 (0.3) |
| SYNE1 | 1333 | 216 (40%) | 6.17 (9) | 173 (76%) | 1286 7.43 (9.8) | 43 (14%) | 47 1.09 (0.3) |
| MUC16 | 1177 | 193 (36%) | 6.1 (8) | 153 (67%) | 1126 7.36 (8.6) | 40 (13%) | 51 1.27 (0.7) |
| CSMD3 | 1141 | 215 (40%) | 5.31 (7.7) | 165 (73%) | 1084 6.57 (8.4) | 50 (16%) | 57 1.14 (0.5) |
| LRP1B | 1088 | 189 (35%) | 5.76 (7.7) | 150 (66%) | 1045 6.97 (8.2) | 39 (12%) | 43 1.1 (0.3) |
| HMCN1 | 1080 | 193 (53%) | 5.59 (7.2) | 160 (70%) | 1042 6.51 (7.7) | 33 (10%) | 38 1.15 (0.4) |
| DST | 1056 | 181 (33%) | 5.83 (8.1) | 153 (67%) | 1024 6.69 (8.6) | 28 (9%) | 32 1.14 (0.4) |

Table S15. Ten most frequently genes percentage, mean, standard deviation, fisher and welch test in Uterine Corpus Endometrial Carcinoma and Uterine Carcinosarcoma with threshold 20 mut/Mb

| Ten most frequently mutated genes | #mutation in all patients | Patients with the mutations (Out of 415) | Mean of mutations per patient (SD) | Patients with mutations and H-TMB level (Out of 84) | Number of mutations in high TMB patients - Mean of mutations per high patient (SD) | Patients with mutations and low TMB level (Out of 331) | Number of mutations in low TMB patients - Mean of mutations per low patient (SD) |
|-----------------------------------|---------------------------|--|------------------------------------|---|--|--|--|
| TTN | 387 | 176 (42%) | 2,2 (2.2) | 71 (84%) | 216 : 3,04 (3.1) | 105 (32%) | 171 : 1,63 (1.1) |
| SYNE1 | 308 | 141 (34%) | 2,18 (1.8) | 65 (77%) | 199 : 3,06 (2.3) | 76 (23%) | 109 : 1,43 (0.8) |
| LRP1B | 266 | 154 (37%) | 1,73 (1.4) | 58 (69%) | 124 : 2,14 (2.1) | 96 (29%) | 142 : 1,47 (0.7) |
| SNHG14 | 260 | 139 (33%) | 1,87 (1.3) | 63 (75%) | 158 : 2,51 (1.5) | 76 (23%) | 102 : 1,34 (0.6) |
| CSMD3 | 248 | 136 (33%) | 1,82 (1.7) | 58 (69%) | 150 : 2,59 (2.3) | 78 (23%) | 98 : 1,26 (0.6) |
| MYHAS | 189 | 99 (24%) | 1,91 (1.7) | 57 (68%) | 141 : 2,47 (2) | 42 (13%) | 48 : 1,14 (0.3) |
| HMCN1 | 186 | 117 (28%) | 1,59 (1.5) | 54 (64%) | 114 : 2,11 (2.1) | 63 (19%) | 72 : 1,14 (0.4) |
| MUC16 | 167 | 144 (27%) | 1,46 (1.1) | 48 (57%) | 87 : 1,81 (1.5) | 66 (20%) | 80 : 1,21 (0.5) |
| DNAH5 | 165 | 97 (23%) | 1,7 (1.4) | 52 (62%) | 112 : 2,15 (1.8) | 45 (13%) | 53 : 1,18 (0.4) |
| SPTA1 | 158 | 110 (26%) | 1,44 (1) | 43 (51%) | 68 : 1,58 (1.3) | 67 (20%) | 90 : 1,34 (0.7) |

Table S16. Ten most frequently genes percentage, mean, standard deviation, fisher and welch test in Stomach adenocarcinoma with threshold 20 mut/Mb

| Ten most frequently mutated genes | #mutation in all patients | Patients with the mutations (Out of 398) | Mean of mutations per patient (SD) | Patients with mutations and high TMB level (Out of 12) | Number of mutations in high TMB patients - Mean of mutations per high patient (SD) | Patients with mutations and low TMB level (Out of 386) | Number of mutations in low TMB patients - Mean of mutations per low patient (SD) |
|-----------------------------------|---------------------------|--|------------------------------------|--|--|--|--|
| ALB | 187 | 133 (33%) | 1.41 (0.8) | 5 (42%) | 12 : 2.4 (1.1) | 128 (33%) | 175 : 1.37 (0.8) |
| TTN | 150 | 109 (27%) | 1.38 (0.7) | 9 (75%) | 18 : 2 (1.6) | 100 (26%) | 132 : 1.32 (0.6) |
| CSMD3 | 121 | 86 (22%) | 1.41 (0.8) | 7 (58%) | 18 : 2.57 (1.9) | 79 (20%) | 103 : 1.3 (0.6) |
| RYR2 | 117 | 90 (23%) | 1.3 (0.7) | 8 (67%) | 20 : 2.5 (1.2) | 82 (21%) | 97 : 1.18 (0.4) |
| MUC19 | 112 | 87 (22%) | 1.28 (0.7) | 9 (75%) | 19 : 2.11 (1.6) | 78 (20%) | 93 : 1.19 (0.4) |
| OBSCN | 187 | 133 (33%) | 1.4 (0.8) | 5 (42%) | 12 : 2.4 (1.1) | 128 (33%) | 175 : 1.4 (0.8) |
| HMCN1 | 101 | 70 (17%) | 1.44 (1) | 7 (58%) | 23 : 3.28 (2.3) | 63 (16%) | 78 : 1.24 (0.5) |
| COL11A1 | 96 | 76 (19%) | 1.26 (0.7) | 7 (58%) | 17 : 2.43 (1.6) | 69 (18%) | 79 : 1.14 (0.4) |
| MUC16 | 96 | 79 (20%) | 1.21 (0.5) | 8 (67%) | 14 : 1.75 (0.9) | 71 (18%) | 82 : 1.15 (0.4) |
| LRP1B | 95 | 76 (19%) | 1.25 (0.7) | 7 (58%) | 15 : 2.14 (1.8) | 69 (18%) | 80 : 1.16 (0.4) |

Table S17. Ten most frequently genes percentage, mean, standard deviation, fisher and welch test in Liver hepatocellular carcinoma with threshold 20 mut/Mb

| Ten most frequently mutated genes | #mutation in all patients | Patients with the mutations (Out of 496) | Mean of mutations per patient (SD) | Patients with mutations and high TMB level (Out of 2) | Number of mutations in high TMB patients - Mean of mutations per high patient (SD) | | Patients with mutations and low TMB level (Out of 494) | Number of mutations in low TMB patients - Mean of mutations per low patient (SD) | |
|-----------------------------------|---------------------------|--|------------------------------------|---|--|-----------|--|--|------------|
| | | | | | | | | | |
| SYNE1 | 55 | 38 (8%) | 1.45 (2.6) | 1 (50%) | 17 | 17 (NA) | 37 (7%) | 38 | 1.03 (0.2) |
| TTN | 54 | 33 (7%) | 1.64 (3.1) | 2 (100%) | 21 | 10.5 (12) | 31 (6%) | 33 | 1.06 (0.2) |
| LRP1B | 41 | 31 (6%) | 1.32 (1.4) | 2 (100%) | 10 | 5 (5.6) | 29 (6%) | 31 | 1.07 (0.3) |
| SNHG14 | 37 | 25 (5%) | 1.48 (2.2) | 2 (100%) | 13 | 6.5 (7.8) | 23 (5%) | 24 | 1.04 (0.2) |
| MUC16 | 35 | 22 (4%) | 1.59 (1.9) | 2 (100%) | 11 | 5.5 (6.4) | 20 (4%) | 24 | 1.2 (0.4) |
| CSMD3 | 32 | 30 (6%) | 1.07 (0.4) | 1 (50%) | 3 | 3 (NA) | 29 (6%) | 29 | 1 (0) |
| HMCN1 | 30 | 27 (5%) | 1.11 (0.4) | 2 (100%) | 4 | 2 (1.4) | 25 (5%) | 26 | 1.04 (0.2) |
| MYHAS | 30 | 21 (4%) | 1.43 (1.1) | 2 (100%) | 7 | 3.5 (3.5) | 19 (4%) | 23 | 1.21 (0.4) |
| KMT2D | 27 | 22 (4%) | 1.23 (0.7) | 1 (50%) | 4 | 4 (NA) | 21 (4%) | 23 | 1.09 (0.3) |
| WASL | 26 | 25 (5%) | 1.04 (0.2) | 0 (0%) | 0 | 0 (0) | 25 (5%) | 26 | 1.04 (0.2) |

Table S18. Ten most frequently genes percentage, mean, standard deviation, fisher and welch test in Prostate adenocarcinoma with threshold 20 mut/Mb

| Ten most frequently mutated genes | #mutation in all patients | Patients with the mutations (Out of 408) | Mean of mutations per patient (SD) | Patients with mutations and high TMB level (Out of 46) | Number of mutations in high TMB patients - Mean of mutations per high patient (SD) | | Patients with mutations and low TMB level (Out of 362) | Number of mutations in low TMB patients - Mean of mutations per low patient (SD) | |
|-----------------------------------|---------------------------|--|------------------------------------|--|--|------------|--|--|-------------|
| | | | | | | | | | |
| TTN | 212 | 130 (32%) | 1,63 (1.4) | 32 (69%) | 80 | 2,5 (2.5) | 98 (27%) | 132 | 1,35 (0,41) |
| SNHG14 | 127 | 98 (24%) | 1,29 (0.7) | 28 (61%) | 48 | 1,71 (1.2) | 70 (19%) | 79 | 1,13 (0,11) |
| SYNE1 | 126 | 82 (20%) | 1,54 (2) | 24 (52%) | 55 | 2,29 (3.5) | 58 (16%) | 71 | 1,22 (0,25) |
| CSMD3 | 102 | 73 (18%) | 1,4 (1.5) | 17 (37%) | 41 | 2,41 (3) | 56 (15%) | 61 | 1,09 (0,08) |
| HMCN1 | 101 | 81 (20%) | 1,25 (0.6) | 20 (43%) | 30 | 1,5 (0.9) | 61 (17%) | 71 | 1,16 (0,21) |
| MYHAS | 97 | 71 (17%) | 1,37 (1.1) | 14 (30%) | 29 | 2,07 (2.2) | 57 (16%) | 68 | 0,37 (1,19) |
| MUC16 | 96 | 72 (18%) | 1,33 (0.8) | 18 (39%) | 35 | 1,94 (1.2) | 54 (15%) | 61 | 1,13 (0,15) |
| RYR2 | 95 | 75 (37%) | 1,27 (0.8) | 23 (100%) | 34 | 1,48 (1.3) | 52 (29%) | 61 | 1,17 (0,18) |
| LRP1B | 90 | 68 (17%) | 1,32 (1) | 17 (37%) | 31 | 1,82 (1.9) | 51 (14%) | 59 | 1,16 (0,13) |
| SYNE2 | 89 | 65 (16%) | 1,37 (0.7) | 23 (50%) | 40 | 1,74 (0.8) | 42 (12%) | 49 | 0,29 (1,67) |

Table S19. Ten most frequently genes percentage, mean, standard deviation, fisher and welch test in Bladder Urothelial Carcinoma with threshold 20 mut/Mb

| Ten most frequently mutated genes | #mutation in all patients | Patients with the mutations (Out of 176) | Mean of mutations per patient (SD) | Patients with mutations and high TMB level (Out of 4) | Number of mutations in high TMB patients - Mean of mutations per high patient (SD) | Patients with mutations and low TMB level (Out of 172) | Number of mutations in low TMB patients - Mean of mutations per low patient (SD) |
|-----------------------------------|---------------------------|--|------------------------------------|---|--|--|--|
| TTN | 91 | 22 (12%) | 4,14 (11.7) | 4 (100%) | 70 : 17,5 (25.8) | 18 (10%) | 21 : 1,17 (0.4) |
| SYNE1 | 48 | 15 (8%) | 3,2 (7.7) | 4 (100%) | 37 : 9,25 (14.6) | 11 (6%) | 11 : 1 (0) |
| MUC16 | 45 | 15 (8%) | 3 (7.5) | 2 (50%) | 32 : 16 (19.8) | 13 (7%) | 13 : 1 (0) |
| HMCN1 | 37 | 11 (6%) | 3,36 (7.2) | 3 (75%) | 28 : 9,33 (13.6) | 8 (5%) | 9 : 1,12 (0.3) |
| LRP1B | 37 | 18 (10%) | 2,05 (3.8) | 4 (100%) | 22 : 5,5 (7.7) | 14 (8%) | 15 : 1,07 (0.03) |
| SNHG14 | 36 | 15 (8%) | 2,4 (4.9) | 4 (100%) | 24 : 6 (9.3) | 11 (6%) | 12 : 1,1 (0.3) |
| MACF1 | 35 | 9 (5%) | 3,89 (6.1) | 4 (100%) | 30 : 7,5 (8.3) | 5 (3%) | 5 : 1 (0) |
| RYR3 | 35 | 14 (8%) | 2,5 (4) | 3 (75%) | 23 : 7,67 (7.2) | 11 (6%) | 12 : 1,09 (0.3) |
| USH2A | 34 | 13 (7%) | 2,61 (5) | 4 (100%) | 24 : 6 (8.7) | 9 (5%) | 10 : 1,11 (0.33) |
| NEB | 33 | 11 (6%) | 3 (6.3) | 4 (100%) | 26 : 6,5 (10.3) | 7 (4%) | 7 : 1 (0) |

Table S20. Ten most frequently genes percentage, mean, standard deviation, fisher and welch test in Pancreatic adenocarcinoma with threshold 20 mut/Mb

| Ten most frequently mutated genes | #mutation in all patients | Patients with the mutations (Out of 494) | Mean of mutations per patient (SD) | Patients with mutations and high TMB level (Out of 19) | Number of mutations in high TMB patients - Mean of mutations per high patient (SD) | Patients with mutations and low TMB level (Out of 475) | Number of mutations in low TMB patients - Mean of mutations per low patient (SD) |
|-----------------------------------|---------------------------|--|------------------------------------|--|--|--|--|
| TTN | 1055 | 341 (69%) | 3,09 (2.3) | 19 (100%) | 135 : 7,1 (3.2) | 322 (68%) | 920 : 2,86 (2) |
| SNHG14 | 585 | 296 (60%) | 1,98 (1.5) | 15 (79%) | 63 : 4,2 (3.4) | 281 (59%) | 522 : 1,86 (1.2) |
| CSMD3 | 473 | 259 (52%) | 1,82 (1.3) | 16 (84%) | 59 : 3,69 (3.3) | 243 (51%) | 414 : 1,7 (1) |
| LRP1B | 468 | 254 (51%) | 1,84 (1.3) | 17 (89%) | 59 : 3,47 (2.7) | 237 (50%) | 409 : 1,72 (1) |
| SYNE1 | 410 | 225 (45%) | 1,82 (1.1) | 18 (95%) | 53 : 2,94 (1.7) | 207 (43%) | 357 : 1,72 (1) |
| MUC16 | 384 | 209 (42%) | 1,84 (1.2) | 17 (89%) | 54 : 3,18 (2.3) | 192 (40%) | 330 : 1,72 (1) |
| RYR2 | 367 | 224 (45%) | 1,64 (1) | 15 (79%) | 44 : 2,93 (1.6) | 209 (44%) | 323 : 1,54 (0.9) |
| USH2A | 327 | 214 (43%) | 1,53 (0.8) | 16 (84%) | 29 : 1,81 (0.8) | 198 (42%) | 298 : 1,5 (0.8) |
| COL22A1 | 285 | 189 (38%) | 1,51 (1) | 11 (58%) | 33 : 3 (1.6) | 178 (37%) | 252 : 1,41 (0.8) |
| SPTA1 | 282 | 191 (39%) | 1,48 (0.8) | 13 (68%) | 25 : 1,92 (1) | 178 (37%) | 257 : 1,44 (0.7) |

Table S21. Ten most frequently genes percentage, mean, standard deviation, fisher and welch test in Lung Squamous Cell Cancer with threshold 20 mut/Mb

| Ten most frequently mutated genes | #mutation in all patients | Number and percentage of patients with the mutations (Out of 512) | Mean of mutations per patient (SD) | Number and percentage of patients with mutations and high TMB level (Out of 29) | Number of mutations in high TMB patients - Mean of mutations per high patient (SD) | Number and percentage of patients with mutations and low TMB level (Out of 483) | Number of mutations in low TMB patients - Mean of mutations per low patient (SD) |
|-----------------------------------|---------------------------|---|------------------------------------|---|--|---|--|
| TTN | 531 | 199 (39%) | 2.67 (2.7) | 29 (100%) | 190 6.55 (4.7) | 170 (35%) | 341 2 (1.3) |
| LRP1B | 481 | 231 (45%) | 2.08 (1.7) | 27 (93%) | 110 4.07 (3) | 204 (42%) | 371 1.82 (1.3) |
| CSMD3 | 455 | 225 (44%) | 2.02 (1.6) | 27 (93%) | 112 4.15 (2.7) | 198 (41%) | 343 1.73 (1) |
| SNHG14 | 441 | 224 (44%) | 1.97 (1.4) | 25 (86%) | 83 3.32 (2.2) | 199 (41%) | 358 1.8 (1.2) |
| RYR2 | 439 | 209 (41%) | 2.1 (1.6) | 29 (100%) | 114 3.93 (3) | 180 (37%) | 325 1.8 (1) |
| MUC16 | 365 | 171 (33%) | 2.13 (1.4) | 27 (93%) | 105 3.89 (2) | 144 (30%) | 260 1.8 (1) |
| USH2A | 342 | 179 (35%) | 1.91 (1.4) | 25 (86%) | 98 3.92 (2.4) | 154 (32%) | 244 1.58 (0.9) |
| SPTA1 | 305 | 174 (34%) | 1.75 (1.1) | 26 (90%) | 75 2.88 (1.6) | 148 (31%) | 230 1.55 (0.8) |
| MYHAS | 248 | 167 (33%) | 1.48 (0.9) | 19 (65%) | 33 1.74 (0.9) | 148 (31%) | 215 1.45 (0.9) |
| COL11A1 | 229 | 144 (28%) | 1.59 (0.9) | 25 (86%) | 62 2.48 (1.3) | 119 (25%) | 167 1.4 (0.6) |

Table S22. Ten most frequently genes percentage, mean, standard deviation, fisher and welch test in Lung Adenocarcinoma with threshold 20 mut/Mb

| Ten most frequently mutated genes | #mutation in all patients | Number and percentage of patients with the mutations (Out of 494) | Mean of mutations per patient (SD) | Number and percentage of patients with mutations and high TMB level (Out of 13) | Number of mutations in high TMB patients - Mean of mutations per high patient (SD) | Number and percentage of patients with mutations and low TMB level (Out of 481) | Number of mutations in L-TMB patients - Mean of mutations per low patient (SD) |
|-----------------------------------|---------------------------|---|------------------------------------|---|--|---|--|
| TTN | 105 | 33 (7%) | 3.18 (7.3) | 11 (85%) | 77 7 (12) | 22 (4%) | 28 1.27 (0.5) |
| SYNE1 | 57 | 27 (5%) | 2.11 (2.7) | 8 (61%) | 34 4.25 (4.4) | 19 (4%) | 23 1.21 (0.4) |
| HMCN1 | 56 | 23 (5%) | 2.43 (3.7) | 9 (69%) | 37 4.11 (5.5) | 14 (3%) | 19 1.36 (0.8) |
| MACF1 | 47 | 22 (4%) | 2.14 (3.2) | 7 (54%) | 28 4 (5.4) | 15 (3%) | 19 1.27 (0.6) |
| KIAA1109 | 45 | 19 (4%) | 2.37 (2.1) | 11 (85%) | 36 3.27 (2.4) | 8 (2%) | 9 1.12 (0.3) |
| TG | 45 | 39 (8%) | 1.15 (0.5) | 4 (31%) | 6 1.5 (1) | 35 (7%) | 39 1.11 (0.4) |
| MUC16 | 44 | 17 (3%) | 2.59 (4.1) | 10 (77%) | 37 3.7 (5.1) | 7 (1%) | 7 1 (0) |
| SNHG14 | 40 | 25 (5%) | 1.6 (1.5) | 7 (54%) | 19 2.71 (2.5) | 18 (4%) | 21 1.67 (0.5) |
| UTP20 | 38 | 16 (3%) | 2.37 (2.6) | 10 (77%) | 30 3 (3.2) | 6 (1%) | 8 1.33 (0.5) |
| MYHAS | 36 | 17 (3%) | 2.12 (2.5) | 11 (85%) | 30 2.72 (3) | 6 (1%) | 6 1 (0) |

Table S23. Ten most frequently genes percentage, mean, standard deviation, fisher and welch test in Thyroid carcinoma with threshold 20 mut/Mb

| Ten most frequently mutated genes | #mutation in all patients | Patients with the mutations (Out of 227) | Mean of mutations per patient (SD) | Patients with mutations and high TMB level (Out of 3) | Number of mutations in high TMB patients - Mean of mutations per high patient (SD) | | Patients with mutations and low TMB level (Out of 224) | Number of mutations in low TMB patients - Mean of mutations per low patient (SD) | |
|-----------------------------------|---------------------------|--|------------------------------------|---|--|------------|--|--|------------|
| | | | | | | | | | |
| MUC16 | 21 | 17 (7%) | 1.23 (0.6) | 3 (100%) | 6 | 2 (1) | 14 (6%) | 15 | 1.07 (0.3) |
| TTN | 21 | 17 (7%) | 1.23 (0.7) | 2 (67%) | 6 | 3 (1.4) | 15 (7%) | 15 | 1 (0) |
| MUC19 | 16 | 12 (5%) | 1.33 (0.6) | 3 (100%) | 4 | 1.33 (0.6) | 9 (4%) | 12 | 1.33 (0.7) |
| RYR1 | 16 | 10 (4%) | 1.6 (0.7) | 3 (100%) | 7 | 2.33 (0.6) | 7 (3%) | 9 | 1.28 (0.5) |
| LRP1 | 15 | 9 (4%) | 1.7 (1) | 1 (33%) | 4 | 4 (NA) | 8 (3%) | 11 | 1.4 (0.5) |
| CSMD1 | 14 | 11 (5%) | 1.27 (0.6) | 2 (67%) | 4 | 2 (1.4) | 9 (4%) | 10 | 1.11 (0.3) |
| ABCA13 | 13 | 12 (5%) | 1.08 (0.3) | 2 (67%) | 3 | 1.5 (0.7) | 10 (4%) | 10 | 1 (0) |
| HMCN1 | 13 | 12 (5%) | 1.08 (0.3) | 2 (67%) | 2 | 1 (0) | 10 (4%) | 11 | 1.1 (0.3) |
| LRP1B | 13 | 10 (4%) | 1.3 (0.7) | 2 (67%) | 4 | 2 (1.4) | 8 (3%) | 9 | 1.12 (0.3) |

Table S24. Ten most frequently genes percentage, mean, standard deviation, fisher and welch test in Adrenocortical carcinoma with threshold 20 mut/Mb

| Ten most frequently mutated genes | #mutations in all patients | Patients with the mutations (Out of 338) | Mean of mutations per patient (SD) | Patients with mutations and high TMB level (Out of 3) | Mutations in high TMB patients - Mean of mutations per high patient (SD) | | Patients with mutations and low TMB level (Out of 335) | Number of mutations in low TMB patients - Mean of mutations per low patient (SD) | |
|-----------------------------------|----------------------------|--|------------------------------------|---|--|------------|--|--|------------|
| | | | | | | | | | |
| TTN | 74 | 48 (14%) | 1.54 (2.3) | 3 (100%) | 20 | 6.67 (9) | 45 (12%) | 54 | 1.2 (0.6) |
| PBRM1 | 64 | 61 (18%) | 1.05 (0.2) | 1 (33%) | 2 | 2 (NA) | 60 (18%) | 62 | 1.03 (0.2) |
| LRP2 | 50 | 43 (13%) | 1.16 (0.5) | 2 (67%) | 4 | 2 (1.4) | 41 (12%) | 46 | 1.12 (0.4) |
| NEB | 39 | 27 (8%) | 1.44 (1.9) | 3 (100%) | 14 | 4.67 (5.5) | 24 (7%) | 25 | 1.04 (0.2) |
| RNR2 | 38 | 37 (11%) | 1.03 (0.2) | 0 (0%) | 0 | 0 (0) | 37 (11%) | 38 | 1.03 (0.2) |
| COL11A1 | 37 | 30 (9%) | 1.23 (0.9) | 1 (33%) | 6 | 6 (NA) | 29 (9%) | 31 | 1.07 (0.3) |
| HMCN1 | 37 | 26 (8%) | 1.42 (1.2) | 2 (67%) | 8 | 4 (4.2) | 24 (7%) | 29 | 1.21 (0.5) |
| VHL | 37 | 37 (11%) | 1 (0) | 0 (0%) | 0 | 0 (0) | 37 (11%) | 37 | 1 (0) |
| SYNE1 | 36 | 30 (9%) | 1.2 (0.8) | 1 (33%) | 5 | 5 (NA) | 29 (9%) | 31 | 1.07 (0.3) |
| SYNE2 | 33 | 28 (8%) | 1.18 (0.6) | 2 (67%) | 5 | 2.5 (2.1) | 26 (8%) | 28 | 1.08 (0.3) |

Table S25. Ten most frequently genes percentage, mean, standard deviation, fisher and welch test in Kidney renal clear cell carcinoma with threshold 20 mut/Mb

| Ten most frequently mutated genes | #mutation in all patients | Patients with the mutations (Out of 287) | Mean of mutations per patient (SD) | Patients with mutations and high TMB level (Out of 4) | Number of mutations in high TMB patients - Mean of mutations per high patient (SD) | Patients with mutations and low TMB level (Out of 283) | Number of mutations in low TMB patients - Mean of mutations per low patient (SD) |
|-----------------------------------|---------------------------|--|------------------------------------|---|--|--|--|
| TTN | 87 | 66 (23%) | 1.32 (0.7) | 4 (100%) | 10 2.5 (1.3) | 62 (22%) | 77 1.24 (0.6) |
| LRP2 | 62 | 51 (18%) | 1.21 (0.5) | 3 (70%) | 5 1.67 (1.1) | 48 (17%) | 57 1.19 (0.4) |
| SYNE1 | 48 | 36 (12%) | 1.33 (0.5) | 4 (100%) | 5 1.25 (0.5) | 32 (11%) | 43 1.34 (0.5) |
| CUBN | 44 | 37 (13%) | 1.19 (0.4) | 1 (25%) | 2 2 (NA) | 36 (13%) | 42 1.17 (0.4) |
| SYNE2 | 44 | 39 (13%) | 1.13 (0.5) | 3 (75%) | 6 2 (1.7) | 36 (13%) | 38 1.05 (0.2) |
| UBR4 | 41 | 35 (12%) | 1.17 (0.4) | 2 (50%) | 3 1.5 (0.70) | 33 (12%) | 38 1.15 (0.4) |
| NEB | 36 | 31 (11%) | 1.16 (0.4) | 2 (50%) | 2 1 (0) | 29 (10%) | 34 1.17 (0.4) |
| PKHD1 | 36 | 33 (11%) | 1.09 (0.3) | 2 (50%) | 2 1 (0) | 31 (11%) | 34 1.1 (0.3) |
| OBSCN | 35 | 33 (11%) | 1.06 (0.2) | 3 (75%) | 5 1.67 (0.6) | 30 (11%) | 30 1 (0) |
| DST | 32 | 29 (10%) | 1.1 (0.3) | 1 (25%) | 2 2 (NA) | 28 (10%) | 30 1.07 (0.3) |

Table S26. Ten most frequently genes percentage, mean, standard deviation, fisher and welch test in Kidney renal papillary cell carcinoma with threshold 20 mut/Mb

| Ten most frequently mutated genes | #mutation in all patients | Patients with the mutations (Out of 465) | Mean of mutations per patient (SD) | Patients with mutations and high TMB level (Out of 256) | Mutations in high TMB patients - Mean of mutations per high patient (SD) | Number and percentage of patients with mutations and low TMB level (Out of 209) | Mutations in low TMB patients - Mean of mutations per low patient (SD) |
|-----------------------------------|---------------------------|--|------------------------------------|---|--|---|--|
| TTN | 1877 | 350 (75%) | 5,36 (7.2) | 239 (93%) | 1685 7,05 (8.2) | 111 (53%) | 192 1,73 (1) |
| MUC16 | 1058 | 286 (62%) | 3,7 (4.8) | 210 (82%) | 951 4,53 (5.3) | 76 (36%) | 107 1,41 (0.7) |
| SNHG14 | 856 | 286 (61%) | 2,99 (3.4) | 208 (81%) | 737 3,54 (3.8) | 78 (37%) | 119 1,52 (0.8) |
| MYHAS | 793 | 266 (57%) | 2,98 (3.4) | 208 (81%) | 713 3,43 (3.7) | 58 (28%) | 80 1,38 (0.6) |
| DNAH5 | 773 | 269 (58%) | 2,87 (3.2) | 203 (79%) | 686 3,38 (3.5) | 66 (31%) | 87 1,32 (0.6) |
| MGAM | 745 | 280 (60%) | 2,66 (3.1) | 203 (79%) | 637 3,14 (3.5) | 77 (37%) | 108 1,4 (0.7) |
| LRP1B | 600 | 234 (50%) | 2,56 (3.2) | 181 (71%) | 535 2,95 (3.5) | 53 (25%) | 65 1,23 (0.6) |
| CSMD2 | 546 | 236 (51%) | 2,31 (2.5) | 184 (72%) | 482 2,62 (2.7) | 52 (25%) | 64 1,23 (0.6) |
| DNAH9 | 449 | 206 (44%) | 2,18 (2.7) | 163 (64%) | 392 2,4 (3) | 43 (20%) | 57 1,32 (0.7) |
| RYR1 | 448 | 213 (46%) | 2,1 (2.4) | 160 (62%) | 385 2,41 (2.7) | 53 (25%) | 63 1,19 (0.4) |

Table S27. Ten most frequently genes percentage, mean, standard deviation, fisher and welch test in Skin Cutaneous Melanoma with threshold 20 mut/Mb