

**Figure S1: Consort Diagram**

**Figure S2: The genomic landscape of BRAF mutant melanoma. A)**

Oncoprint highlighting the top 30 most frequent genes that are differentially altered between melanomas with Class 1/2/3 BRAF mutations. **B)** Histogram indicating the incidence of gene alterations within each BRAF class for the top 30 most frequently altered genes. **C)** The filtered list of genes that were significantly differentially altered according to BRAF Class 1/2 and 1/3 across all melanomas (n=31 and n= 153 respectively,  $Q < 0.05$ ) was subjected to pathway analysis using the using MSigDB Hallmark algorithm. All pathways that were over-represented in this list of genes are indicated in blue, red, and green ( $P < 0.05$  &  $Q < 0.05$ ,  $P < 0.05$  &  $Q < 0.2$ , and  $P < 0.1$  &  $Q < 0.2$  respectively).

**Figure S3: The genomic landscape of BRAF mutant Colorectal tumors. A)**

Oncoprint highlighting the top 30 most frequent genes that are differentially altered between tumors with Class 1/2/3 BRAF mutations. **B)** Histogram highlighting the incidence of gene alterations within each BRAF class. **C)** The filtered list of genes that were significantly differentially altered according to BRAF Class 1/2 and 1/3 status across CRCs (n=4 and n=44 respectively,  $Q < 0.05$ ) was subjected to pathway analysis using the using MSigDB Hallmark algorithm. All pathways that were over-represented in this list of genes ( $P < 0.05$  &  $Q < 0.05$ ) are indicated.

**Figure S4: The genomic landscape of BRAF mutant NSCLC tumors. A)**

Oncoprint highlighting the top 30 most frequent genes that are differentially altered between tumors with Class 1/2/3 BRAF mutations. **B)** Histogram highlighting the incidence of gene alterations within each BRAF class. **C)** The filtered list of genes that were significantly differentially altered according to BRAF Class 1/2 and 1/3 status across NSCLC (n=6 and n=9 respectively,  $Q < 0.05$ ) was subjected to pathway analysis using the using MSigDB Hallmark algorithm. All pathways that were over-represented in this list of genes are indicated in red and blue ( $P < 0.05$  &  $Q < 0.1$ , and  $P < 0.1$  &  $Q < 0.1$ , respectively).

**Figure S5: Gene ontology analysis on altered genes from all BRAF mutant cancer types. A.** Top 18 altered genes were inputted for Gene Ontology Biological Process analysis ( $p < 2.01 \times 10^{-7}$ ,  $q < 0.001$ , hide gene-unconnected terms) **B.** Top 59 genes altered were inputted for Gene Ontology Biological Process analysis ( $p < 2.13 \times 10^{-20}$ ,  $q < 0.001$ , hide gene-unconnected terms).

**Figure S6: Violin plots displaying the distribution of age at sequencing according to BRAF Class 1, Class 2, Class 3 and Fusion in all cancers, melanoma, CRC, non-small cell lung cancer (NSCLC) and other cancers (all cancers excluding melanoma, CRC and NSCLC). P-value was calculated using two-way ANOVA test for each table.**

**Table Legends**

**Table S1: Incidence and Classification of BRAF alterations** BRAF Class was determined by protein changes shown in the table. The table describes the occurrence of each protein change from the 5120 BRAF mutant samples used for analyses.

**Table S2: Co-Mutations across all cancer types in BRAF Class 1, 2 and 3** Genomic alterations for genes obtained from the GENIE v12 database for BRAF Classes 1, 2 and 3 within all cancer types. The table includes all listed genes, no modifications from the database.



**Table S3: Co-Mutations across all cancer types in BRAF Class 1 and 2** Genomic alterations for genes obtained from the GENIE v12 database for BRAF Classes 1 and 2 within all cancer types. The table includes all listed genes, no modifications from the database.

**Table S4: Filtered Co-Mutations across all cancer types in BRAF Class 1 and 2** Genomic alterations for genes obtained from the GENIE v12 database for BRAF Classes 1 and 2 within all cancer types. The table shows genes with minimum 15 samples mutated in BRAF Class 1/2,  $p < 0.05$ , and  $q < 0.05$ .

**Table S5: Co-Mutations across all cancer types in BRAF Class 1 and 3** Genomic alterations for genes obtained from the GENIE v12 database for BRAF Classes 1 and 3 within all cancer types. The table includes all listed genes, no modifications from the database.

**Table S6: Filtered Co-Mutations across all cancer types in BRAF Class 1 and 3** Genomic alterations for genes obtained from the GENIE v12 database for BRAF Classes 1 and 3 within all cancer types. The table shows genes with minimum 15 samples mutated in BRAF Class 1/3,  $p < 0.05$ , and  $q < 0.05$ .

**Table S7: Co-Mutations across BRAF Class 1 and 2 melanomas** Genomic alterations for genes obtained from the GENIE v12 database for BRAF Classes 1 and 2 within melanoma. The table includes all listed genes, no modifications from the database.

**Table S8: Filtered Co-Mutations across BRAF Class 1 and 2 melanomas** Genomic alterations for genes obtained from the GENIE v12 database for BRAF Classes 1 and 2 within melanoma. The table shows genes with minimum 15 samples mutated in BRAF Class 1/2,  $p < 0.05$ , and  $q < 0.05$ .

**Table S9: Co-Mutations across BRAF Class 1 and 3 melanomas** Genomic alterations for genes obtained from the GENIE v12 database for BRAF Classes 1 and 3 within melanoma. The table includes all listed genes, no modifications from the database.

**Table S10: Filtered Co-Mutations across BRAF Class 1 and 3 melanomas** Genomic alterations for genes obtained from the GENIE v12 database for BRAF Classes 1 and 3 within melanoma. The table shows genes with minimum 15 samples mutated in BRAF Class 1/3,  $p < 0.05$ , and  $q < 0.05$ .

**Table S11: Co-Mutations across BRAF Class 1 and 2 colorectal cancers** Genomic alterations for genes obtained from the GENIE v12 database for BRAF Classes 1 and 2 within melanoma. The table includes all listed genes, no modifications from the database.

**Table S12: Filtered Co-Mutations across BRAF Class 1 and 2 colorectal cancers** Genomic alterations for genes obtained from the GENIE v12 database for BRAF Classes 1 and 2 within melanoma. The table shows genes with minimum 15 samples mutated in BRAF Class 1/2,  $p < 0.05$ , and  $q < 0.05$ .

**Table S13: Co-Mutations across BRAF Class 1 and 3 colorectal cancers** Genomic alterations for genes obtained from the GENIE v12 database for BRAF Classes 1 and 3 within melanoma. The table includes all listed genes, no modifications from the database.

**Table S14: Filtered Co-Mutations across BRAF Class 1 and 3 colorectal cancers** Genomic alterations for genes obtained from the GENIE v12 database for BRAF Classes 1 and 3 within melanoma. The table shows genes with minimum 15 samples mutated in BRAF Class 1/3,  $p < 0.05$ , and  $q < 0.05$ .

**Table S15: Co-Mutations across BRAF Class 1 and 2 NSCLC** Genomic alterations for genes obtained from the GENIE v12 database for BRAF Classes

1 and 2 within melanoma. The table includes all listed genes, no modifications from the database.

**Table S16: Filtered Co-Mutations across BRAF Class 1 and 2 NSCLC** Genomic alterations for genes obtained from the GENIE v12 database for BRAF Classes 1 and 2 within melanoma. The table shows genes with minimum 15 samples mutated in BRAF Class 1/2,  $p < 0.05$ , and  $q < 0.05$ .

**Table S17: Co-Mutations across BRAF Class 1 and 3 NSCLC** Genomic alterations for genes obtained from the GENIE v12 database for BRAF Classes 1 and 3 within melanoma. The table includes all listed genes, no modifications from the database.

**Table S18: Filtered Co-Mutations across BRAF Class 1 and 3 NSCLC** Genomic alterations for genes obtained from the GENIE v12 database for BRAF Classes 1 and 3 within melanoma. The table shows genes with minimum 15 samples mutated in BRAF Class 1/3,  $p < 0.05$ , and  $q < 0.05$ .

**Table S19: RNA expression Heatmap Genes CRC** Gene list of RNA expression from BRAF mutant CRC heatmap. Genes are ordered from top to bottom as seen on heatmap. Cutoffs of  $\text{baseMean} > 50$ ,  $\text{absolute Logfold} > 2$ , and  $\text{padj} < 0.01$  were used to obtain these genes. Log fold denotes the BRAF Class 1 vs BRAF Class 2&3 mutants.

**Table S20: RNA expression Heatmap Genes NSCLC** Gene list of RNA expression from BRAF mutant Non-Small Cell Lung cancer heatmap. Genes are ordered from top to bottom as seen on heatmap. Cutoffs of  $\text{baseMean} > 50$ ,  $\text{absolute Logfold} > 2$ , and  $\text{padj} < 0.01$  were used to obtain these genes. Log fold denotes the BRAF Class 2&3 vs BRAF Class 1 mutants.

**Table S21: RNA expression Heatmap Genes Melanoma** Gene list of RNA expression from BRAF mutant Melanoma heatmap. Genes are ordered from top to bottom as seen on heatmap. Cutoffs of  $\text{baseMean} > 50$ ,  $\text{absolute Logfold} > 2$ , and  $\text{padj} < 0.01$  were used to obtain these genes. Log fold denotes the BRAF Class 1 vs BRAF Class 2&3 mutants.