

Supplementary Tables

Table S1. The code for this analysis is available at <https://bitbucket.org/evertbosdriesz/cgc-multi-omics>, in the notebook src/R/combined-pca.Rmd

Sheet	Description
RNA	It contains PCA loading and log ₂ -fold-changes of mRNA compared to T=0 h.
PROT	It contains PCA loading and log ₂ -fold-changes of proteins compared to T=0 h.
PHOS	It contains PCA loading and log ₂ -fold-changes of phosphosites compared to T=0 h.

Table S2. It contains differential mRNA expression analysis and pathways analysis in **BRAF(V600E) CRC cell lines**. The code for this analysis is available at <https://bitbucket.org/evertbosdriesz/cgc-multi-omics>, in the notebook src/R/validation/dge-vaco-snuc5-km20.Rmd

Sheet	Description
BRAFiEGFRi_CTRL	Differential expression analysis of BRAFi+EGFRi compared to Control for SNU-C5, VACO432 KM-20.
BRAFi_CTRL	Differential expression analysis of BRAFi compared to Control for SNU-C5, VACO432 KM-20.
pathways_BRAFiEGFRi	Mean log ₂ -fold-changes of mRNAs per geneset which are significantly enriched amongst the upregulated proteins upon BRAFi+EGFRi in the WiDr cell line. The p-value indicates if the mean log ₂ -fold-change is significantly larger than 0.
pathways_BRAFi	Mean log ₂ -fold-changes of mRNAs per geneset which are significantly enriched amongst the upregulated proteins upon BRAFi in the WiDr cell line. The p-value indicates if the mean log ₂ -fold-changes is significantly larger than 0.

Table S3. Differential mRNA and protein expression between PTPN11 WT and PTPN11 KO. The code for this analysis is available at <https://bitbucket.org/evertbosdriesz/cgc-multi-omics>, in the notebook src/R/ptpn11-proteins-down.Rmd

Sheet	Description
RNA	Differential expression results of PTPN11 WT vs KO of all transcripts
PROT	Differential expression results of PTPN11 WT vs KO of all proteins
prot-ptpn11-down	Results of the differential expression analysis of proteins and mRNAs when comparing PTPN11 KO to PTPN11 WT cells, while correcting for time-point and treatment. P-values were adjusted for multiple testing using the Benjamini-Hochberg procedure.
enrichment-ptpn11-down	Results of enrichment analysis of selected genes using the MSigDB Hallmark gene sets. Enrichment analysis was done using the Fisher-exact test with all genes measured on both protein and mRNA level as population. Genes were selected based on being strongly downregulated on the protein but not mRNA level. P-values were adjusted for multiple testing using the Benjamini-Hochberg procedure.

Table S4. Full clustering and enrichment results from correlation clustering.

The code for this analysis is available at <https://bitbucket.org/evertbosdriesz/cgc-multi-omics>, in the notebook src/R/correlation-clustering.Rmd.

Sheet	Description
PHOSPHO_CLUSTERS	List of clusters assigned to phosphosites.
PHOSPHO_ENRICHMENT	Enrichment of kinase-substrates in the phosphoproteomic clusters. Genesets are all (predicted) substrates of a kinase.

PROT_CLUSTERS	List of clusters assigned to proteins.
PROT_ENRICHMENT	Enrichment of transcription factor-target gene in the proteomics clusters. Genesets are all target genes of a transcription factor. This sheet is empty because there were no significant enrichments.
PROT_ENRICHMENT_HALLMARKS	Enrichment of the MSigDB Hallmark genesets in the proteomics clusters.
RNA_CLUSTERS	List of clusters assigned to transcripts.
RNA_ENRICHMENT	Enrichment of transcription factor-target gene in the transcriptomics clusters. Genesets are all target genes of a transcription factor.
RNA_ENRICHMENT_HALLMARKS	Enrichment of the MSigDB Hallmark genesets in the transcriptomics clusters.

Table S5. Differential mRNA and protein expression between BRAFⁱ and Control WiDr cells after 48 h. The code for this analysis is available at <https://bitbucket.org/evertbosdriesz/cgc-multi-omics>, in the notebook src/R/enrichment-p-ctr.Rmd.

Sheet	Description
PROT	Differential expression analysis of proteins.
RNA	Differential expression analysis of transcripts.
ENRICHMENT_PROT_UP	Enrichment analysis of proteins differentially expressed based p-value (FDR < 0.05) and effect size (log ₂ -fold-changes > 0) by using the MSigDB Hallmark, KEGG, and Reactome genesets.

ENRICHMENT_PROT_DOWN	Enrichment analysis of proteins differentially expressed based p-value (FDR < 0.05) and effect size (\log_2 -fold-changes < 0) by using the MSigDB Hallmark, KEGG, and Reactome genesets.
ENRICHMENT_RNA_UP	Enrichment analysis of transcripts differentially expressed based p-value (FDR < 0.05) and effect size (\log_2 -fold-changes > 0) by using the MSigDB Hallmark, KEGG, and Reactome genesets. This sheet is empty because there were no significant enrichments.
ENRICHMENT_RNA_DOWN	Enrichment analysis of transcripts differentially expressed based p-value (FDR < 0.05) and effect size (\log_2 -fold-changes < 0) by using the MSigDB Hallmark, KEGG, and Reactome genesets.
PROT_GENESET_RNA	Mean \log_2 -fold-changes of mRNAs per geneset which are significantly enriched amongst the upregulated proteins. The p-value indicates if the mean \log_2 -fold-changes is significantly larger than 0.

Table S6. Differential mRNA and protein expression between BRAFⁱ+EGFRⁱ and Control cells after 48 h. The code for this analysis is available at <https://bitbucket.org/evertbosdriesz/cgc-multi-omics>, in the notebook src/R/enrichment-pg-ctr.Rmd.

Sheet	Description
PROT	Differential expression analysis of proteins
RNA	Differential expression analysis of transcripts

ENRICHMENT_PROT_UP	Enrichment analysis of proteins differentially expressed based p-value (FDR < 0.05) and effect size (\log_2 -fold-changes > 0) by using the MSigDB Hallmark, KEGG, and Reactome genesets.
ENRICHMENT_PROT_DOWN	Enrichment analysis of proteins differentially expressed based p-value (FDR < 0.05) and effect size (\log_2 -fold-changes < 0) by using the MSigDB Hallmark, KEGG, and Reactome genesets.
ENRICHMENT_RNA_UP	Enrichment analysis of transcripts differentially expressed based p-value (FDR < 0.05) and effect size (\log_2 -fold-changes > 0) by using the MSigDB Hallmark, KEGG, and Reactome genesets. This sheet is empty because there were no significant enrichments.
ENRICHMENT_RNA_DOWN	Enrichment analysis of transcripts differentially expressed based p-value (FDR < 0.05) and effect size (\log_2 -fold-changes < 0) by using the MSigDB Hallmark, KEGG, and Reactome genesets.
PROT_GENESET_RNA	Mean \log_2 -fold-changes of mRNAs per geneset which are significantly enriched amongst the upregulated proteins. The p-value indicates if the mean \log_2 -fold-changes is significantly larger than 0.

Table S7. proteinGroups. The table contains the list of identified and quantified proteins by MaxQuant using the integrated Andromeda search engine, and a mutant-modified Homo sapiens Swiss-Prot database for the (phospho)protein database search. Each protein is

provided with the accession code, the number of unique peptides assigned, the percentage sequence coverage and the quantification value.

Table S8. Phospho (STY)Sites. The table contains the list of identified and quantified phosphosites by MaxQuant using the integrated Andromeda search engine, and a mutant-modified Homo sapiens Swiss-Prot database for the (phospho)protein database search. Each phosphosite is provided with the position, the accession code, the localization probability calculated with PEP, peptide sequence window containing the phosphorylation, and the quantification value.

Table S9. modificationSpecificPeptides. The table contains the list of modified peptides identified by MaxQuant using the integrated Andromeda search engine, and a mutant-modified Homo sapiens Swiss-Prot database for the (phospho)protein database search. Each peptide is provided with the modification type, the accession code, the number of modifications, the mass value, and the quantification value.