

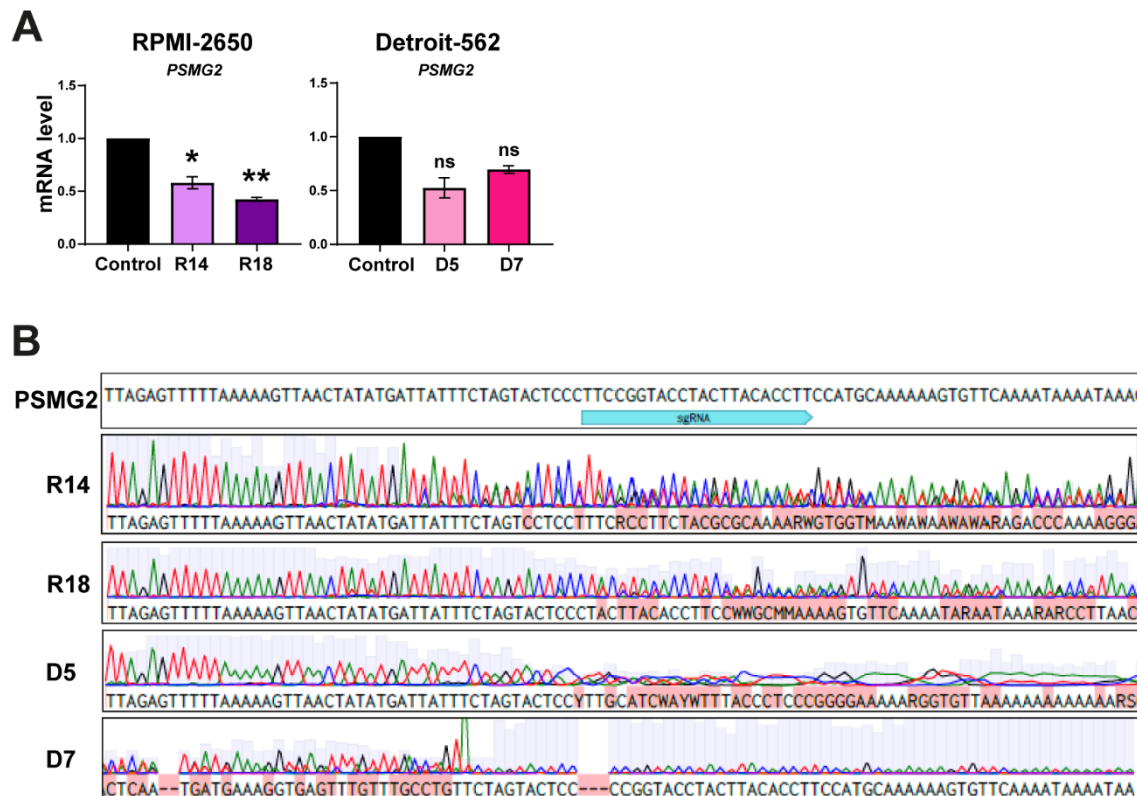


Figure S1. (A) Validation of the reduction in PSMG2 expression in CRISPR PSMG2 cells of the RPMI-2650 and Detroit-562 head-neck cancer cell lines by RT-PCR. **(B)** Part of DNA sequence which containing the sgRNA sequence (indicated in blue) in original sequence of PSMG2 to compare with the sequence of R14, R18, D5 and D7 clones. Behind the sgRNA sequence, it is found nucleotide sequence modified by cas9 cut site (indicated in red). The mean of a minimum of 3 independent experiments performed in triplicate $\pm$ standard error is represented in all experiments. Statistical analysis was performed with the t-Student test, ns: non-significant, * $p < 0.05$, ** $p < 0.01$.

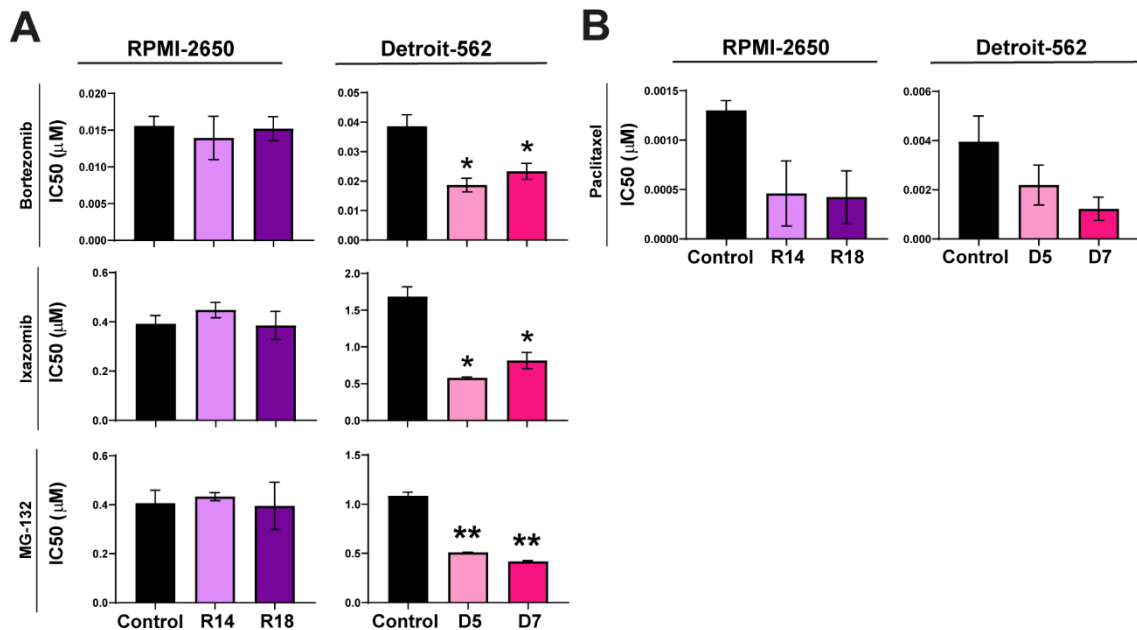


Figure S2. Impact of PSMG2 dowregulation on chemotherapeutic drug response. (A-C) IC50 of proteasome inhibitors **(A)** and paclitaxel **(B)** in control and PSMG2 CRISPRs. The mean of a minimum of 3 independent experiments performed in triplicate $\pm$ standard error is shown in all experiments. Statistical analysis was performed with Student's t test, ns: non-significant, * $p < 0.05$.

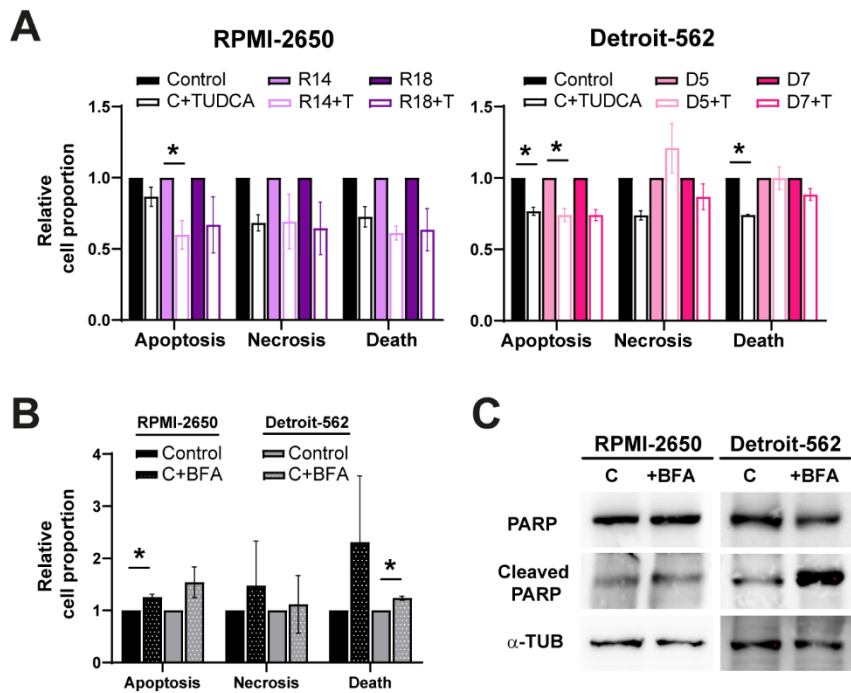


Figure S3. Analysis of cell death induced by ER stress modulation using TUDCA and BFA. (A) Proportion of cell death in RPMI-2650 and Detroit-562 control cells, CRISPRs PSMG2 and control and CRISPRs cells treated with TUDCA (+T) by FACS. **(B)** Proportion of cell death in RPMI-2650 and Detroit-562 control cells and cells treated with BFA by FACS. **(C)** Western blot analysis of PARP in control and BFA-treated cells. C/Control (parental cell line), +T (cell line treated with TUDCA), +BFA (cell line treated with BFA). The mean of a minimum of 3 independent experiments performed in triplicate $\pm$ standard error is represented in all experiments. Statistical analysis was performed with Student's t test, * $p < 0.05$, ** $p < 0.01$.

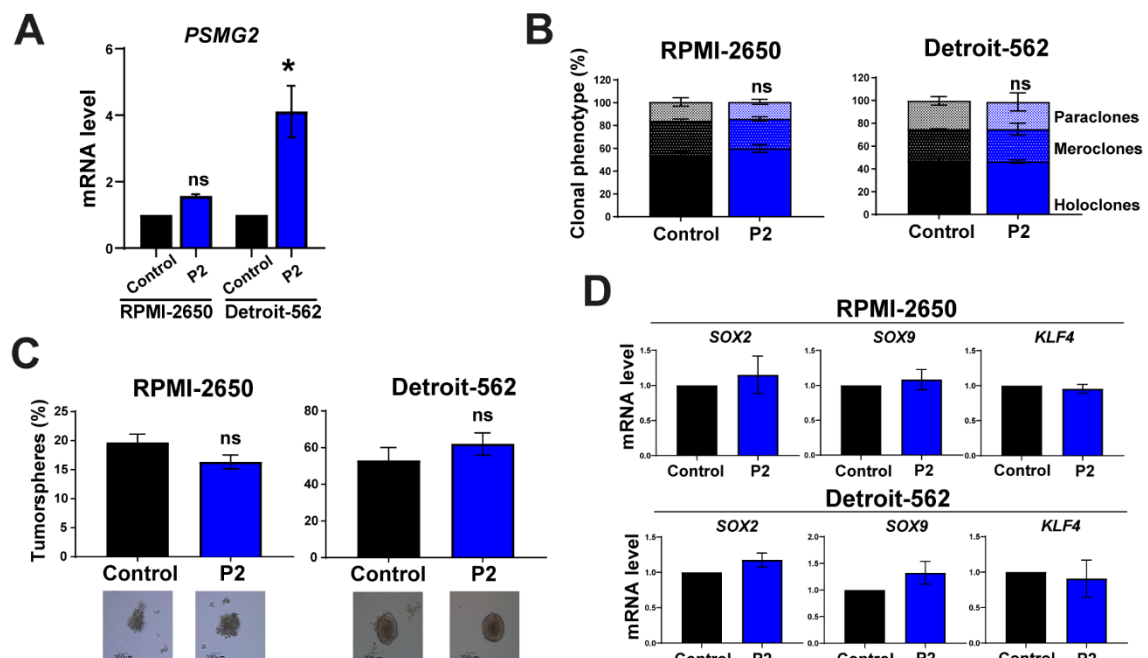


Figure S4 (A) Validation of the overexpression of PSMG2 in cells of the RPMI-2650 and Detroit-562 head-neck cancer cell lines by RT-PCR. **(B)** Percentages of holoclones, meroclones and paraclones generated by RPMI-2650 and Detroit-562 control and overexpressed PSMG2 cell lines seeded at low density over 15 days. **(C)** Percentages of tumorspheres formed from the whole population of RPMI-2650 and Detroit-562

control and overexpressed PSMG2 cell lines. Representative images of the tumorspheres are shown (scale bars: 200 μ m). **(D)** Measurement of *SOX2*, *SOX9*, *KLF4* and *NANOG* expression levels by RT-qPCR in RPMI-2650 and Detroit-562 control and overexpressed PSMG2 cell lines. Graphs represent mRNA levels in overexpression of PSMG2 cells normalized to the mRNA levels of control cells. The mean of a minimum of 3 independent experiments performed in triplicate $\pm$ standard error is represented in all experiments. Statistical analysis was performed with the t-Student test, ns: non-significant.

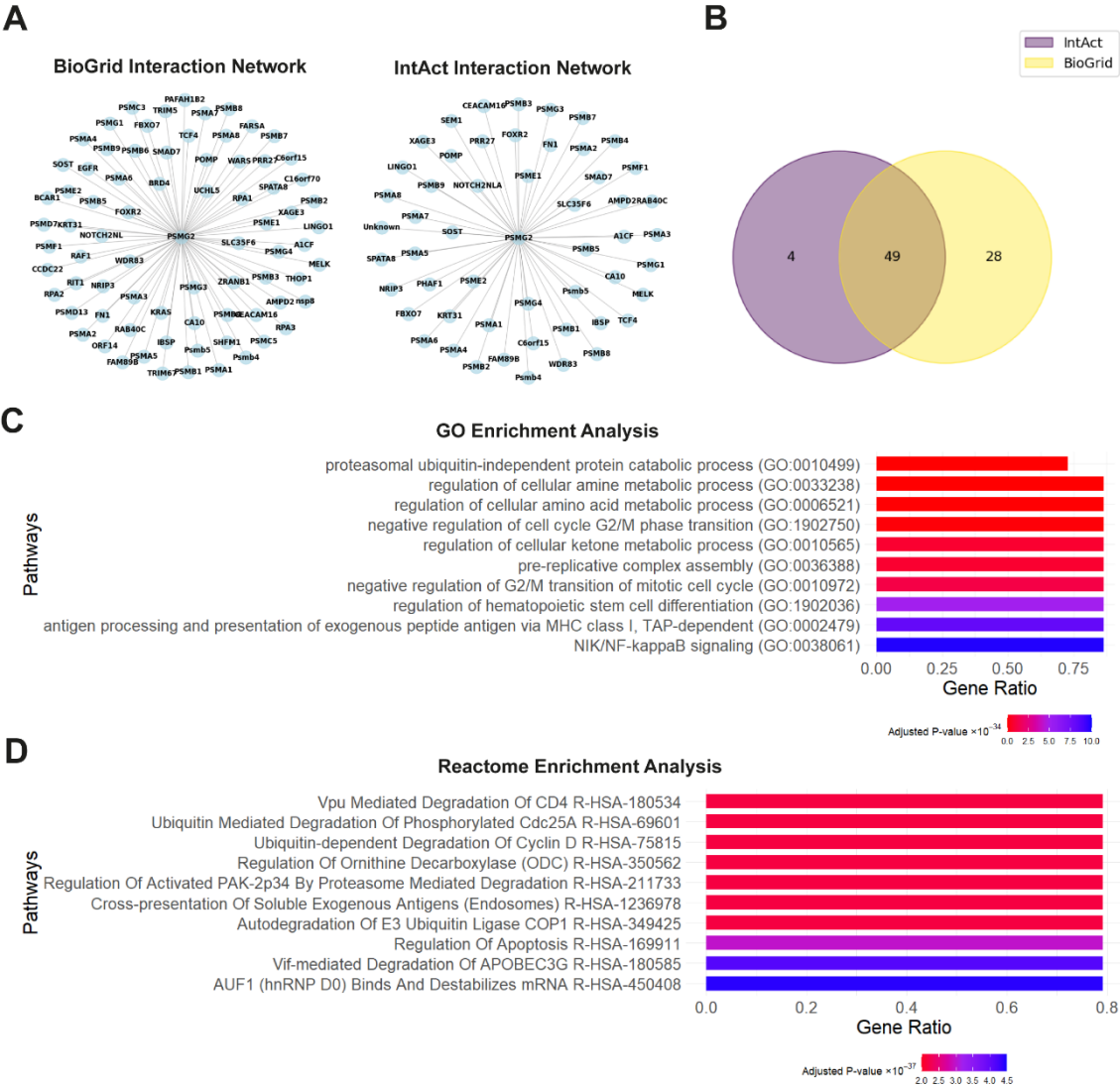


Figure S5. Integration of PSMG2 interactome data from BioGRID and IntAct databases. (A) Network interaction graphs were generated for each database to illustrate the connectivity and relationships among the interacting proteins. **(B)** A Venn diagram was constructed to visualize the overlap of interactions identified in both databases. **(C-D)** Genes that were common to both datasets were selected for Gene Ontology (GO) enrichment analysis **(C)** and Reactome pathway analysis **(D)**.

Acronyms

ACC	Adrenocortical Carcinoma
BLCA	Bladder Urothelial Carcinoma
BRCA	Breast Invasive Carcinoma
CESC	Cervical and Endocervical Cancer
CHOL	Cholangiocarcinoma
COAD	Colon Adenocarcinoma
DLBC	Diffuse Large B-cell Lymphoma
ESCA	Esophageal Carcinoma
GBM	Glioblastoma Multiforme
HNSCC	Head and Neck Squamous Cell Carcinoma
KICH	Kidney Chromophobe
KIRC	Kidney Renal Clear Cell Carcinoma
KIRP	Kidney Renal Papillary Cell Carcinoma
LAML	Acute Myeloid Leukemia
LGG	Lower Grade Glioma
LIHC	Liver Hepatocellular Carcinoma
LUAD	Lung Adenocarcinoma
LUSC	Lung Squamous Cell Carcinoma
MESO	Mesothelioma
OV	Ovarian Serous Cystadenocarcinoma
PAAD	Pancreatic Adenocarcinoma
PCPG	Pheochromocytoma and Paraganglioma
PRAD	Prostate Adenocarcinoma
READ	Rectum Adenocarcinoma
SARC	Sarcoma
SKCM	Skin Cutaneous Melanoma
STAD	Stomach Adenocarcinoma
TGCT	Testicular Germ Cell Tumors
THCA	Thyroid Carcinoma
THYM	Thymoma
UCEC	Uterine Corpus Endometrial Carcinoma
UCS	Uterine Carcinosarcoma
UVM	Uveal Melanoma