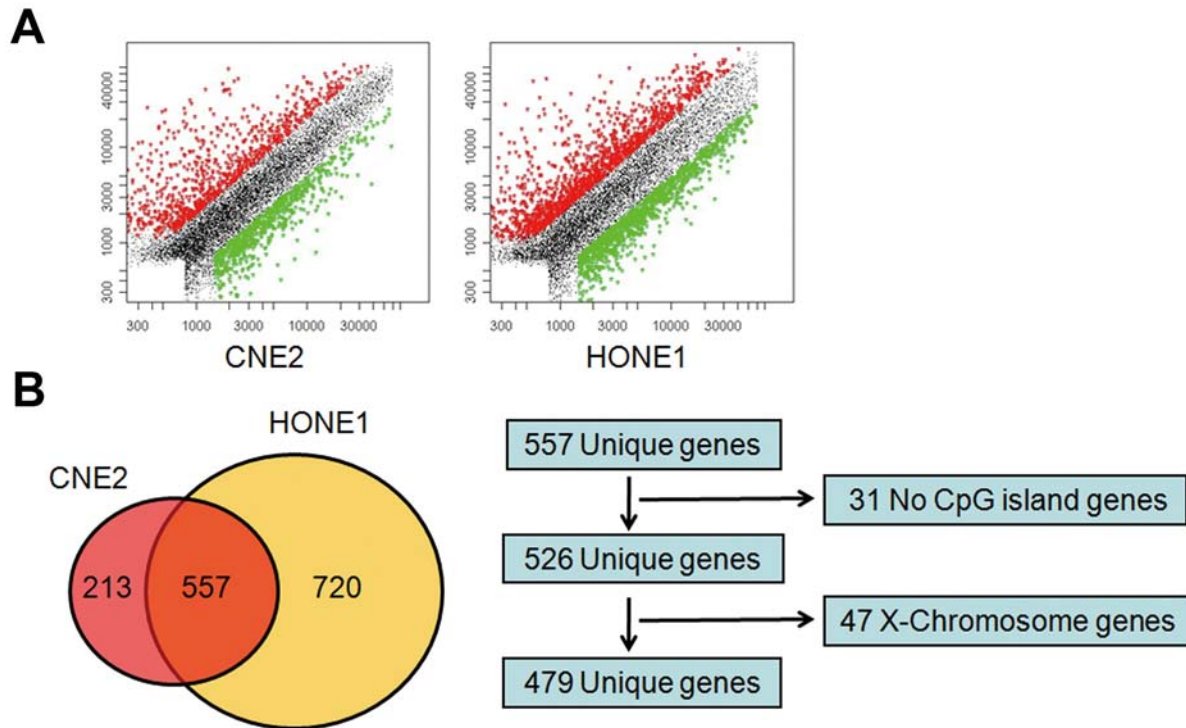
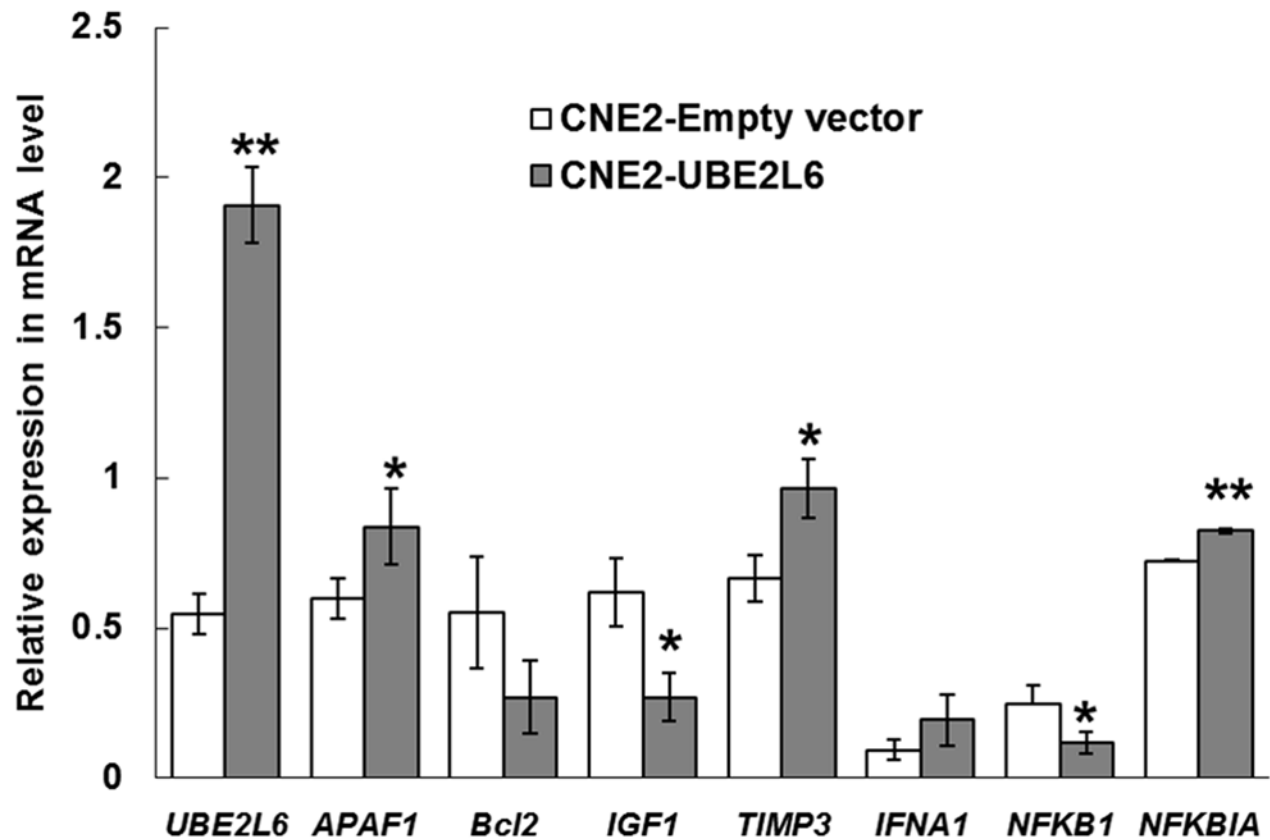


SUPPLEMENTARY FIGURES AND TABLES

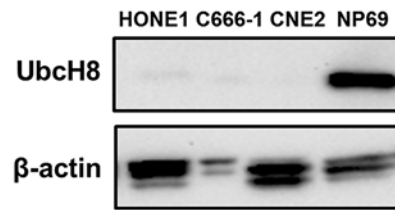


Supplementary Figure S1: Genome-wide screening of genes inactivated by DNA methylation in multiple NPC cells. **A.** Dot plots show the expression levels of genes altered by 5-aza-dC and TSA. Red dots represent genes, the expression levels of which were up-regulated after treatment, while green dots show genes that were down-regulated. **B.** Venn diagram depicts the distribution of up-regulated genes in two NPC cell lines. 557 genes were significantly up-regulated by 5-aza-dC and TSA in two NPC cell lines. Genes without CpG island in the 5' region and genes located at the X chromosome were excluded, after which 479 candidates remained for further investigation.

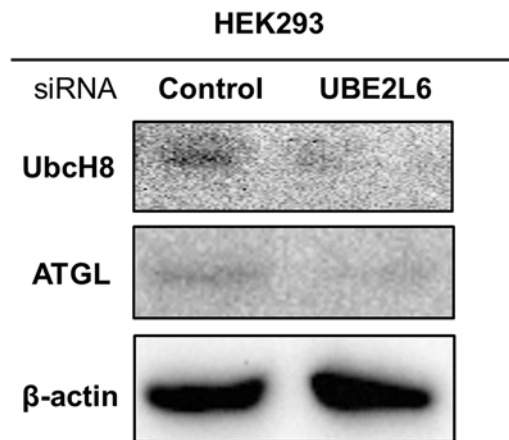


Supplementary Figure S2: Gene expression analysis in CNE2 cells upon ectopic introduction of *UBE2L6* by semi-quantitative RT-PCR. Relative expression levels obtained from 3 independent experiments are shown in bar graphs. There was a significant difference in expression of 7 genes, including apoptotic protease activating factor 1 (*APAF1*), B-cell CLL/lymphoma 2 (*Bcl-2*), insulin growth factor 1 (*IGF1*), human tissue inhibitor of metalloproteinases-3 (*TIMP3*), interferon alpha 1 (*IFNA1*), nuclear factor of kappa light polypeptide gene enhancer in B-cells inhibitor, alpha (*NFKBIA*) and nuclear factor of kappa light polypeptide gene enhancer in B-cells 1 (*NFKB1*).

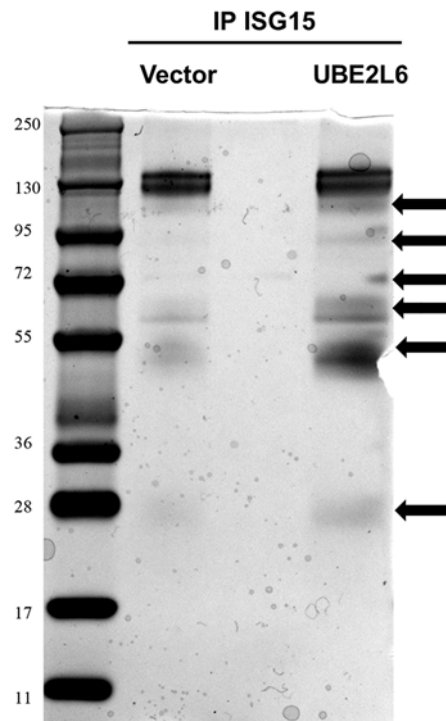
* $p < 0.05$, ** $p < 0.01$.



Supplementary Figure S3: UbcH8 was downregulated in NPC cell lines. Western blot analysis of the UbcH8 expression in NPC cell lines (HONE, C666-1 and CNE2) and normal epithelial cell line NP69. β -actin was used as an endogenous control.



Supplementary Figure S4: Knock-down of UbcH8 in HEK 293 cells downregulates the expression of ATGL. Cells were transfected with either siRNA against UbcH8 (siUbcH8) or siRNA against irrelevant RNA (siControl). Forty-eight hours post-transfection cells were lysed and samples of total cell proteins were analysed by Western blot, for UbcH8 and ATGL expression. β -Actin was used as an endogenous control.



Supplementary Figure S5: Exogenous expression of UbcH8 induces increased ISG15ylation. CNE2 cells were transfected with either an empty vector or an *UBE2L6*-coding plasmid. Forty-eight hours post-transfection, cells were lysed and immunoprecipitation with ISG15 antibody were performed. ISG15ylated proteins were resolved on a polyacrylamide gel in denaturing condition and stained with silver. Arrows point to the ISG15ylated proteins.

Supplementary Table S1: Primer sequences used in this study

	Primers	sequence(5'-3')
RT-PCR	UBE2L6	F:AAACACTGGCCGATCACCT
		R:TGACCAAGATATCCTCCTCTGT
	APAF1	F:CTGCCATAAGCCCTGTCCTCCA
		R:ATTCTGGGTCCGGGTGCAGTT
	Bcl-2	F:TGGCAGGAGGGGCAAGGTGGA
		R:GCAGGTCGGTGAGCTGCCAGGATG
	IGF1	F:CGGCAAAGAAGTTGAACGAGTGG
		R:TGCACAAGGGAGGTGTGTTGGTAA
	TIMP3	F:GTAACCTGCGGATTGGCTTCG
		R:GAAGCGGGTCACCTGGTCAGT
	IFNA1	F:GTGGTGGGACCAGGGAGATTG
		R:TTCAGCGTATCCGAGGACTTCTT
	NFKB1	F:CCGGCTCGCAGGTCTCAAC
		R:TCACCGGGCCGAGGTTAC
	NFKBIA	F:GCTCTCCTGTTGTGCTTCTCCACT
		R:AGCTGCTTAATCTCCTCAGGGATG
GAPDH	F:CTTCTGAGTTGCCAGGAGACCACT	
	R:TCAACCACTCACACACACAACCA	
Real-time RT-PCR	ISG15	F:CAACAAGCCCACAGGGTATGGCT
		R:TGGGCATGTCCGGTGTGGCGCT
	GAPDH	F:CAGGAGTTTGGGTCTGCAGTGTGA
		R:TGGAGGAGGGAGTCCGATAGAAGC
Methylation Specific PCR	UBE2L6-M	F:GCATTGGCAAAGGTTCGATTTGG
		R:TCGCCGTGGACAGAGCAAGTT
	UBE2L6-U	F:CGAAGGTCCTACAGGGCCACAAC
		R:CTCGCAAGAAATGCCACATGAA
Bisulphite sequencing	UBE2L6-BISQ	F:AAGCTCACTGGCATGGCCTT
		R:CTCTCTCCTCTTGTGCTCTTG