

Supplemental Tables & Figures

Supplemental Table S1: Data extraction of the included articles in the scoping review. The 38 articles present the list of HPV-positive (+) and HPV-negative (-) mutated genes. 2 articles out of the 38 articles screened have included both lists of genes. However, the rest included HPV + mutated genes which this scoping review mainly highlights. 330 genes were identified and submitted to enriched analysis. *TP53* (n= 22) and *PIK3CA* (n= 20) genes were the most mutated genes in HPV-related OPC cases.

AUTHOR, YEAR	HPV + GENES MUTATED	HPV - GENES MUTATED
1. R. Alex Harbison et al., 2018	KMT2D, FGFR3, CYLD, EP300, PIK3CA, RB1, PEG3, STAT3, TTSC2, B2M, CREBBP, FBXW7, FLT1, NCOR1, NSD1, PTEN, USP9X, BRIP1, NBN, NFE2L2, TACC3, ARID1B, ARID5B, DDR2, EPHA2, FANCA, KDM5C, LRRK2, MAP2K2, MAPK1, NOTCH3, PTPRD, SMAD2, SYK, TRAF3, TRRAP, FLT1, IDH2, AR, ASXL1, ATM, AXIN1, BAP1, BCR, CIC, ELF3, FANCA, FAT1, FLT4, GRIN2A, HDAC4, HIF1A, IFNGR1, KMT2D, LRP2, MAP3K5, MED12, MTOR, NBN, PIK3R6, RB1, SRC, TACC3, TRRAP, TSC2, XPO1. RECURRENT OPSCCS:- TP53, CASP8, FAT1, HLA-A, AJUBA, AND NSD1.	
2. Chung, C. H. et al., 2015	IK3CA, SOX2, MLL2 (KMT2D), RB1, BCL6, EP300, NOTCH1, PTEN, FGFR3, ASXL1, KLHL6, FBXW7, TP53, ATM, BRCA2, BRIP1 (BACH1), LRP1B, ATRX, KDM6A, BRCA1, BLM, JAK2, NF1, HRAS, MYC, ATR, FGFR19, FGFR3, FGFR4, RICTOR	TP53, CDKN2A/B, FGF19, FGF3, FGF4, PIK3CA, CCND1, NOTCH1, LRP1B, SOX2, MLL2 (KMT2D), EGFR, KLHL6, BCL6, ATR, NFE2L2, NOTCH2, MYC, FGFR1, ATRX, JAK2, SMAD4, RICTOR, ZNF703, BRCA2, FOXL2, PRKDC, GPR124, KDM6A, APC.
3. Doerstling, S. et al., 2023	ATM, CCND1, CDKN2A, RB1, EGFR, FBXW7, FGFR1, FGFR2, FGFR3, IDH1, KRAS, NRAS, HRAS, NOTCH1 AKT1, MTOR, PIK3CA, PTEN, TP53, AR, ALK, BRAF, BRCA1, BRCA2, CDK/RB PATHWAY (CCND1, CDKN2A, RB1), FGFR1-4, FLT3, JAK2, MET, MLH1, MSH2, MSH6, PI3K PATHWAY (AKT1, MTOR, PIK3CA, PTEN).	
4. Dogan, S. et al., 2019	TP53, SOX2, CDKN2A/2B, PIK3CA, TP63, KMT2D, NOTCH1, FAT1, 11Q13 GENE CLUSTER (FGF3/FGF4/FGF19/CCND1), FOXA1, NOTCH PATHWAY GENES (NOTCH1, NOTCH2, NOTCH3, NOTCH4, EP300, FBXW7, SPEN, KDM5A), HISTONE MODIFIERS (KMT2D, CREBBP, KMT2C, EP300, KMT2A), NFE2L2, KEAPI, CUL3, EGFR, ERBB2, FGFR1, FGFR3, FOXA1, TERT, NKX2-1, FGFR1, PMA1P1, ERBB2, EGFR, YAP1, ATM, MYC, KEAP1, CASP8, CUL3, JAK3, MAPK13, FOXA1, HRAS, CCND1, PIK3/AKT/MTOR PATHWAY, FAT1, RUNX1.	
5. Dubot, C. et al., 2018	CDKN2B, RB1,MDM2, RICTOR, PIK3, KRAS, NRAS, MAPK, AJUBA, SYNE2, USP9X, KDM6A, NSD1, LRP1B. CELL CYCLE PATHWAY (TP53, CCND1, CDKN2A), PI3K/AKT/MTOR PATHWAY (PIK3CA), TYROSINE KINASE RECEPTORS (EGFR, FGFR1), CELL DIFFERENTIATION (FAT1, NOTCH1).	
6. Gleber-Netto, F. O. et al., 2018	TP53, NOTCH1, CDKN2A, NOTCH2, PIK3CA, FAT1, FBXW7, KEAP1, NFE2L2, NSD1, TP63, EGFR, HRAS, CASP8, CCND1, TGFBR2	
7. Gronhoj, C. et al., 2018	APOB, BIRC6, SPTBN1, FAT2, KMT2A, FAT1, BPTF, TRIO, HERC2, KALRN, ZNRF3, BNC2, NOTCH2, FGFR2, SMAD2, AR, SIN3A, PTCH1, DNMT3A, ARHGAP35, F5, IGF1R, CATSPER1, IQGAP1, SFMBT2, MET, DUBP1, TENN2, TSC1, ARID5B, FAT2, FNDC1, BIRC6, PTPN14, QSER1, ALS2CL, PIK3CB, ARID2, NOTCH3, APOB, FGFR1, NF2, NRXN3, MYH9, PRPF8, FOXP1, PEX2, PBRM1, IPO7, SPTA1, TRIO, ABCG1, TIP2, EP300, RET, SLX4, AKT2, FN1, HCFC1, PCDH18, WHSC1, BPTF, CREBBP	
8. Haft, S. et al., 2019	PIK3CA, KMT2C, FBXW7, FGFR3, CREBBP, FAT1, NSD1, KMT2D, NOTCH1, CASP8, CLTCL1, EPHA2, HLA-A, HRAS, PDE4DIP, PTCH1, PTEN, ZNF750, ADCY4, AJUBA, ATM, CTCF, CUL3, FANCA, MET, LRP1B, CASZ1, CYLD, EP300, KALRN, MACF1, ASXL3, CSMD3, DST, FLNC, HUWE1, KIAA1407, ASPM, DNAH5, FAM135B, HERC1, HFM1, LRRC37B, MAP1B, MUC4, MUC5B, POLR3A, TRAF3, SERPINB5, USP6, FLG	
9. Koncar, R. F. et al., 2017	ABL1, AKT1, ALK, APC, ATM, BRAF, BRCA1, BRCA2, CDH1, C-KIT, CMET, CSF1R, CTNNB1, EGFR, ERBB2, ERBB4, FBXW7, FGFR1, FGFR2, FLT3, GNA11, GNAQ, GNAS, HNF1A, HRAS, IDH1, JAK2, JAK3, KDR, KRAS, MLH1, MPL, NOTCH1, NPM1, NRAS, PDGFRA, PIK3CA, PTEN, PTPN11, RB1, RET, SMAD4, SMARCB1, SMO, STK11, TP53, VHL	
10. Labarge, B. et al., 2022	FLG, PIK3CA, MUC12, ZNF750, USE1, KMT2D, MUC6, TP63, SLitrk3, NLRC5, MORN1, EFNB2, HLA-A, KRTAP1-1, B2M, PXN, CDKN2A, RB1, TRAF3, PTEN	
11. Lim, S. M. et al., 2019 Multicentric study	TP53, CDKN2A, CCND1, PIK3CA, KMT2C, FAT1, RELN, FAT4, CDKN2B, EGFR, KMT2D, NFE2L2, ADGRV1, NOTCH1, FAT2, CTTN, MYC, GNAS, EPHB4, ASXL3, CHD4, SOX2, ASXL1, KEAP1, AR, NOTCH2, KLHL6, TERT, KRAS, PTEN, MAP3K9, CDH9, CDH1, IDH1, HPV	
12. Qin, T. et al., 2018	PDE4DIP, FAT1, NOTCH2, AHNAK, NUMA1, MKI67, ABCC3, ABCC1, PRKDC, TP53, MUC16, NRG1, TIAM1, NOTCH3, CASP8, CEP290, KLRC2, MAP3K1, NBAS, PTPRB	
13. Reder, H. et al., 2019	TP53, RB1, STK11, CDH1, HRAS, KRAS, NRAS, FAT1, PIK3CA, PIK3R1, PTEN, FANCA, FBXW7, CYLD, BCL6, TP63, TAF1, EP300, DDX3X, NOTCH1, JAK1, JAK2, PDGFRA.	
14. Reder, H. et al., 2021.	TP53, RB1, STK11, CDH1, HRAS, KRAS, NRAS, FAT1, PIK3CA, PIK3R1, PTEN, FANCA, FBXW7, CYLD, BCL6, TP63, TAF1, EP300, DDX3X, NOTCH1, JAK1, JAK2, PDGFRA.	
15. Saba, N. F. et al., 2020	PIK3CA, FGFR3, ZNF750, SYNE2, FLG, SYNE1, PLXNA1, PLEC, HERC1, ZFHX4, VPS8, USH2A, TRAF3, TACC2, RYR3, PTEN, OTOG, LAMA2, KIAA1109, JK, FBN3, EP300, DNAH5, DNAH14,	
16. Wahle, B. M. et al., 2022	PIK3CA, FGFR3, ZNF750, SYNE2, FLG, SYNE1, PLXNA1, PLEC, HERC1, ZFHX4, VPS8, USH2A, TRAF3, TACC2, RYR3, PTEN, OTOG, LAMA2, KIAA1109, JK, FBN3, EP300, DNAH5, DNAH14,	

	CUX1, BIRC5, AK5, SMARCAL1, PIK3R1, IQCG, METTL24, FBXW7, B2M, NRAS, IFI27, HLA-B, FGF2, AKT1, FGF8	
17. Stransky, N. et al., 2011	TP53, CDKN2A, CASP8, FAT1, NOTCH1, PTEN, SYNE1, HRAS, PIK3CA, MED1, MLL2, TP63, IRF6, EZH2, SYNE2, NOTCH3, RIPK4, NOTCH2, DICER1, RB1.	
18. Williams, E. A. et al., 2021	PIK3CA, KMT2D, FBXW7, PTEN, KMT2C, TP53, BCL2L1, NOTCH1, RB1, HPV16	
19. Antonsson, A. et al., 2016	EVER1 & EVER2	
20. Barten, M. et al., 1995	P53 MUTATION	
21. Benzerdjeb, N. et al., 2021	TP53 MUTATIONS.	
22. Chen, Z. et al., 2021	FAT1 MUTATIONS.	
23. Chiosea, S. I. et al., 2013	PIK3CA, HRAS AND PTEN GENE MUTATIONS.	
24. Ekalaksananan, T. et al., 2020	P53 R282 GENE MUTATIONS.	
25. Fallai, C. et al., 2009	TP53 MUTATIONS.	
26. Farnebo, L. et al., 2015	DNA REPAIR GENES XPC, XPD, XRCC1, XRCC3 AND HPV, P53 MUTATIONS.	
27. Hong, A. et al., 2016	P53 MUTATIONS.	
28. Cortelazzi, B. et al., 2015	PIK3CA, PTEN, IGF1R, IGF1, IGF2, HER2, HER3.	
29. De Carvalho, A. C. et al., 2019	TP53 MUTATIONS.	
30. Friedland, P. et al., 2012	EGFR, KRAS, BRAF.	
31. Ghosh, A. et al., 2013	PHF2 , FANCC, PTCH1 ALTERATIONS	
32. Gross, A. M. et al., 2014	TP53 MUTATIONS, CASP8	
33. Huang, C. et al., 2019	NSD1, NOTCH1, TP53, CDKN2A, PIK3CA	
34. Licitra, L. et al., 2006	TP53 MUTATIONS.	
35. Mazurek, A. M. et al., 2016	KRAS, EGFR GENE MUTATIONS	
36. Saba, N. F. et al., 2015 Pilot Study	CDKM2C, SYK, WNT10B, CEBPA, MAP3K8, FGR, GATA1, OL4, PDGFA, CDKN2A, E2F2, TP53, PIK3CA, FGFR3, RB1, MET	
37. Sewell, A. et al., 2014	PIK3CA MUTATIONS	
38. Shaikh, H. et al., 2021	PIK3CA, KMT2D, TP53, LOH, KMT2C, CYLD, FBXW7, NOTCH1, RB1, PIK3CB, PTEN, B2M, NF1, ASXL1, KDM6A, PIK3R2, CHEK2, NSD1, FAT1, MAPK1, CREBBP, TERT, TP53, PIK3CA, RB1, NOTCH1, ARID1A, NF1, KMT2D, FAT1, LOH, ASXL1, KMT2C, CDKN2A, FBXW7, ATM, FGFR3, KDM6A, FANCM, EP300, B2M, KRAS.	TP53, TERT, PIK3CA, NOTCH1, FAT1, CDKN2A, LOH, KMT2D, RB1, KMT2C, ASXL1, NF1, EP300, ARID1A, FBXW7, NFE2L2, CYLD, NSD1, KDM6A, PBRM1, FGFR3, HRAS. TP53, TERT, CDKN2A, LOH, KMT2D, NOTCH1, PIK3CA, FAT1, ARID1A, ASXL1, KMT2C, NSD1, FBXW7, EP300, RB1, CREBBP, NF1, CYLD, KDM6A, HRAS, PTEN, NFE2L2.

Supplementary Table S2: Distribution of the OSCC cases according to demographic, lifestyle, and clinical variables.

Variable	Category	Paraffin-embedded samples n(%)	HELA2 n (%)		<i>P-value</i>
			Negative	Positive	
Age	< 50 year	8 (15.4)	7 (16.7)	1 (10)	0.599
	≥ 50 year	44 (84.6)	35 (83.3)	9 (90)	
Gender	Male	31 (59.6)	26 (61.9)	5 (50)	0.500
	Female	21 (40.4)	16 (38.1)	5 (50)	
Smoking habit	No	23 (44.2)	21 (53.8)	2 (22.2)	0.087
	Yes	29 (55.8)	18 (46.2)	7 (77.8)	
Alcohol consumption	No	16 (37.2)	13 (37.1)	3 (37.5)	0.985
	Yes	27 (62.8)	22 (62.9)	5 (62.5)	
Clinical stage	T1+T2	32 (61.5)	29 (69)	3 (30)	0.023
	T3+T4	20 (38.5)	13 (31)	7 (70)	
Lymph nodes	N0	40 (76.9)	34 (81)	6 (60)	0.158
	N+	12 (23.1)	8 (19)	4 (40)	
Recurrence or metastasis	No	40 (76.9)	31 (73.8)	9 (90)	0.275
	Yes	12 (23.1)	11 (26.2)	1 (10)	
Status	Alive	45 (86.5)	37 (88.1)	8 (80)	0.500
	Dead	7 (13.5)	5 (11.9)	2 (20)	

Supplemental Figure S1: shows list of all genes mutated with highlighting on the most cited genes which are *TP53* (n=22), *PIK3CA* (n=20), *PTEN* (n=16), *NOTCH1* (n=14), *RB1* (n=13), *FAT1* (n=13), *FBXW7* (n=12), *HRAS* (n=10), *KRAS* (n=10) and *CDKN2A* (n=10). Different colour codes representing the 38 articles screened to show which gene was collected from which article. The most frequently mutated gene is *TP53* followed by *PIK3CA*. Genes for cell survival and proliferation (*TP53*, *HRAS* & *PIK3CA*), cell-cycle control (*CDKN2A*), cellular differentiation (*NOTCH1*), and adhesion and invasion signalling (*FAT*). Tumor suppressor Genes (*FAT1*, *NOTCH1* & *CDKN2A*).









