

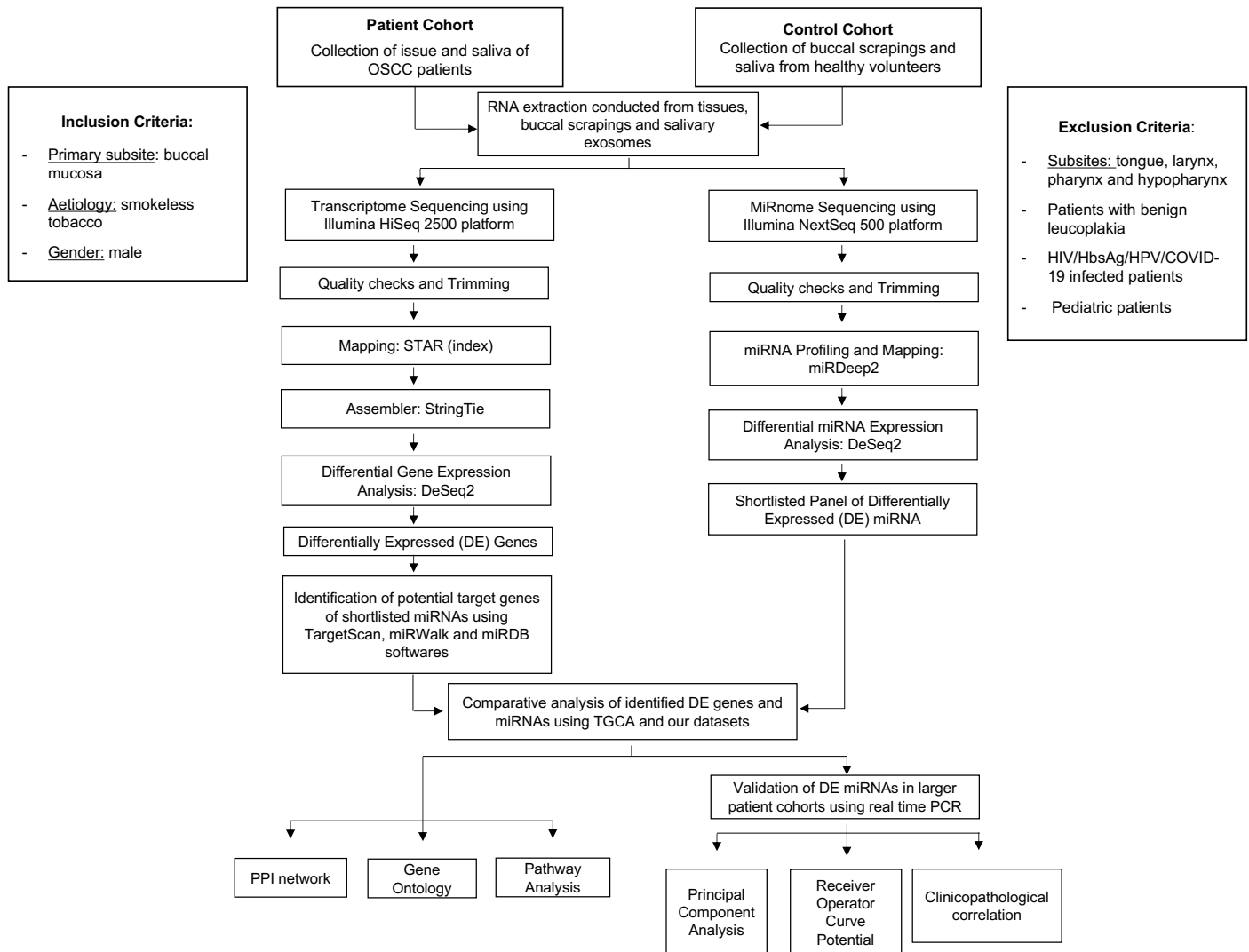


Figure S1: Overview of the study design. This figure explains the design of this study. It shows the sequencing and data analysis pipeline that was followed.

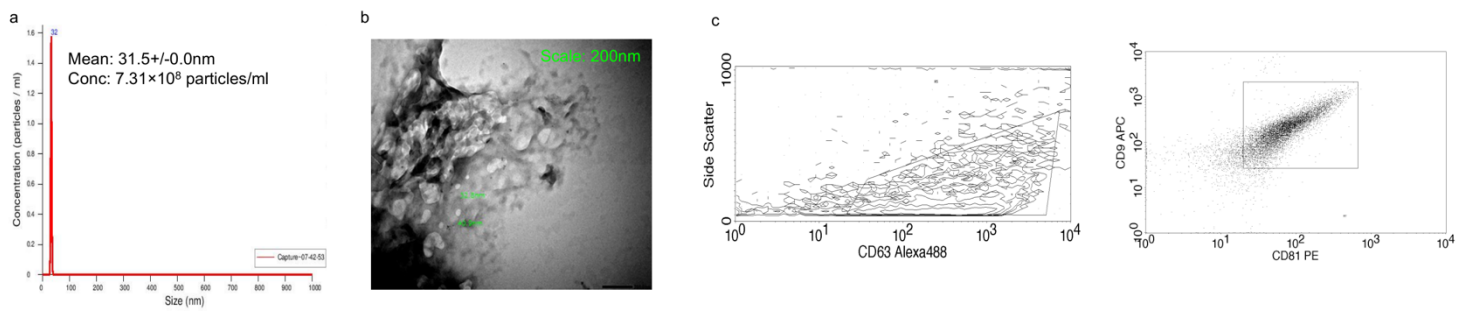


Figure S2: Characterization of salivary exosomes from OSCC patients. (a) Estimation of concentration and size of salivary exosomes derived from OSCC patients using Nanoparticle Tracking Analysis (NTA). The y-axis represents signal intensity and the x-axis indicates the size distribution of particles in NTA. (b) Representative TEM images of exosomes from OSCC patients, (Scale: 200 nm); (c) Representative plots of salivary exosomes stained with anti-CD63-Alexa fluor 488, anti-CD81-PE, and anti-CD9-APC antibodies analyzed by flow cytometry.

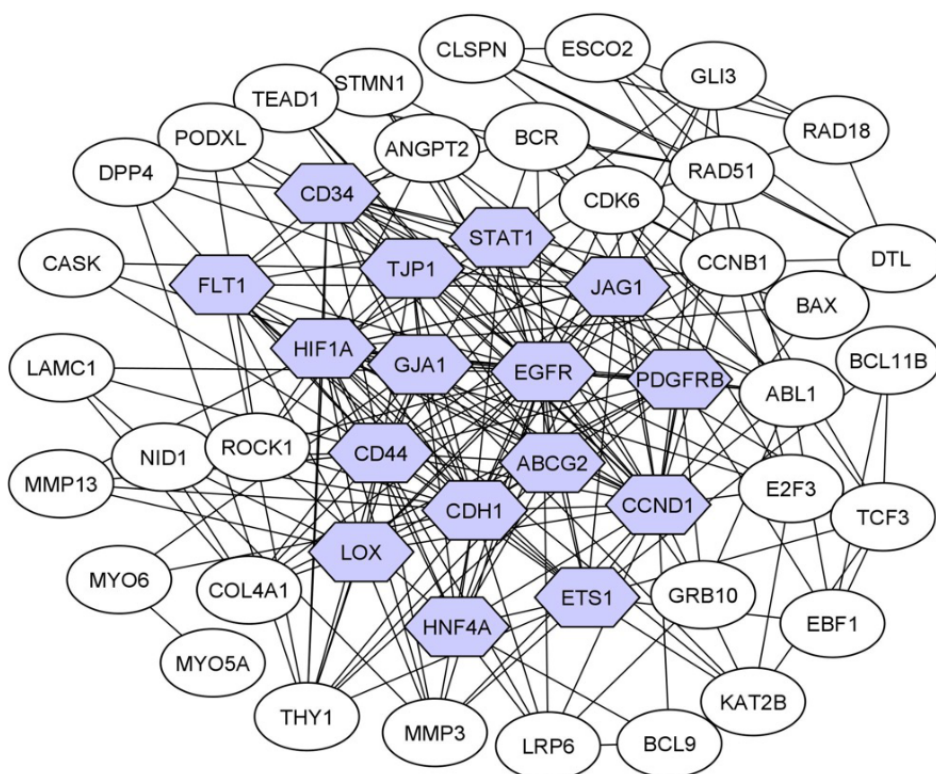


Figure S3: The gene network of mRNAs constructed using Cytoscape with Maximum Clique Centrality (MCC) Score. Protein-Protein interaction network generated in Cytoscape using STRING plugin. The hub gene analysis was performed by cytoHubba. The blue-colored nodes represent the 16 nodes with the highest MCC score.

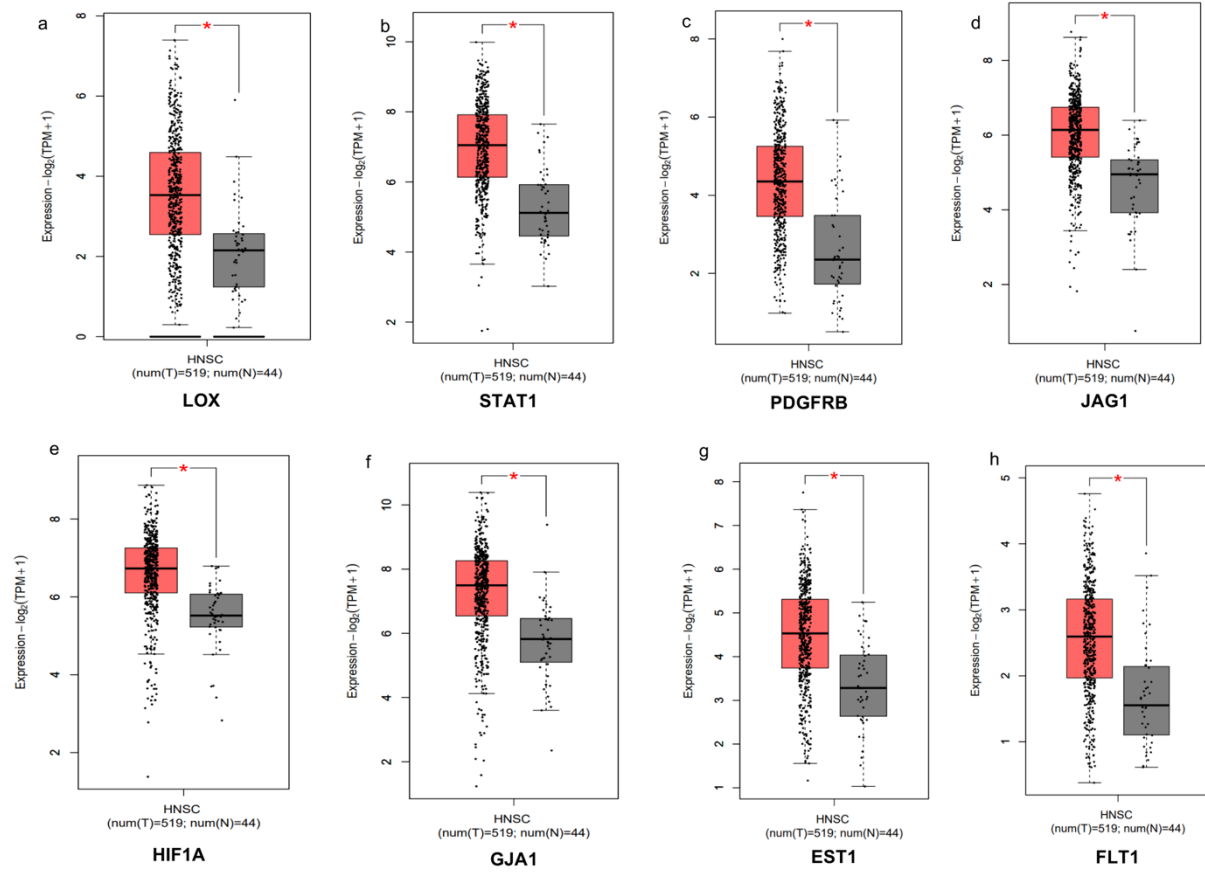


Figure S4: Differential expression of top hub genes based on the HNSCC TCGA dataset using the GEPIA platform. Differential expression of (a) LOX (b) STAT1 (c) PDGFRB (d) JAG1 (e) HIF1 α (f) GJA1 (g) EST1 (h) FLT1 that were found to be significantly expressed in the HNSCC TCGA dataset as compared to their representative controls ($p < 0.01$), $-\log_2(\text{TPM} + 1)$.

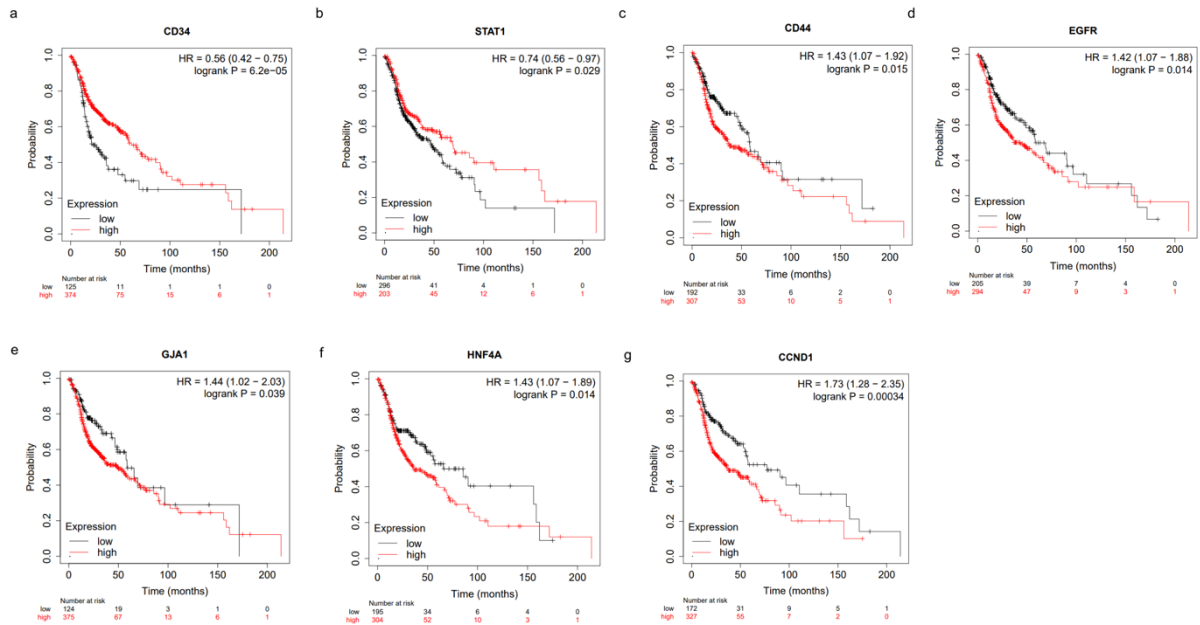


Figure S5: Overall survival analysis of hub genes performed using the GEPIA platform. Overall survival analyses performed using the GEPIA platform where patients with hub genes **(a)** CD34 **(b)** STAT1 **(c)** CD44 **(d)** EGFR **(e)** GJA1 **(f)** HNF4A **(g)** CCND1 expression above the median are indicated by red lines, and black lines indicate patients with hub gene expression below the median. Log-rank $p < 0.05$ was considered to indicate a statistically significant difference.

Table S1: The top enriched networks generated by IPA comprising of different sets of differentially expressed genes.

ID	Molecules in Network	Score	Focus Molecules	Top Diseases and Functions
1	ADAM9,CALU,CDH1,CITED2,CTTNBP2NL,DAB2,DLGAP1,DPP4,ERK1/2,FMNL2,GJA1,GRB10,Growthhormone,LMNB2,MMD,Mmp,MYO6,NETO2,NRIP1,NUAK1,PAXBP1,PDE4D,PODXL,PP2A,PRKAA,PTGFR,S1PR1,SET,Shc,SPTBN1,STAT5a/b,STK38L,STRN,TJP1,T RPM7	43	28	[Cancer, Organismal Injury and Abnormalities , Respiratory Disease]
2	ABCE1,ABCG2,ACSL4,AHI1,ANKHD1/ANK HD1-EIF4EBP3, B4GALT6, CCND1, CDK4/6,CDK6,COL4A1,DTL,E2f,EGFR, estrogen receptor, G3BP1, GRHL1, Hdac,JAG1,KLF9,KLHL24,LRP6,MAP2K1/2, Mek,MGAT1,PITX2,PTPRK,RAD18,RAD51,R af,SACS,SMAD1,Smad2/3,SRGAP1,TEAD1,T HNSL1	41	27	[Cellular Response to Therapeutics, Embryonic Development, Organismal Development]
3	143,ABL1,B4GALT5,BCL11B,BCR,CAMK2G, CARD10,caspase,CD44,Creb,ETS1,FSCN1,GLI 3,LAMC1,Mapk,MMP13,MMP3,MYL12A,NFk B (complex),PDGFRB,Pka,Pka catalytic subunit,Pkc(s),PPP3CB,PRLR,RAS,RNF216,R OCK,ROCK1,RTKN,SRGAP3,ST3GAL5,TAX 1BP1,THY1,WASF1	36	25	[Cancer, Cellular Movement, Gastrointestinal Disease]
4	AARS1,Actin,BCR (complex),CCNB1,CDCA3,DGKH,E2F3,EGLN ,ELK4,ERK,FLNB,Gamma tubulin,Histone h3,HTATSF1,IgG,Jnk,KAT2B,MAP3K4,MTOR C1,NECTIN1,P-TEFb,PAN2,PDGF BB,PGM1,PPP1CC,Rb,RNA polymerase II,SLC38A2,SMAD5,STMN1,TCF3,Tgf beta,TM4SF18,TMOD3,ZNF337	28	21	[Cancer, Hematological Disease, Immunological Disease]
5	AKAP12,Akt,Alphatubulin,ANGPT2,APOL4,B 4GAT1,CD3,DLC1,DPYSL2,EEA1,F Actin,FLT1,Focal-adhesion kinase,Gsk3,HIF1A,Hsp27,Hsp70,Hsp90,KANK 2,LOX,MAP3K5,NUCKS1,P38 MAPK,PAPSS2,PI3K(complex),PI3K (family),PTGS1,RALGDS,Ras homolog,SLC4A7,SLC7A1,SRC (family),STAT1,TUBGCP3,Vegf	26	20	[Cancer, Cardiovascular System Development and Function, Tissue Morphology]
6	BCL9,BICC1,BTF3,CDON,CSNK1D,CTNNB1 ,CUL1,CXCL14,CYP51A1,EID1,EXT1,FER,F GD4,GPR161,GPS1,HAMP,HIC1,HMG CoA synthase,HMGB3,IDI1,KIF3A,LRP4,LZTS2,M ARK1,MDFIC,NUCKS1,OSBPL1A,PLPPR4,P	17	15	[Embryonic Development, Organ Development,

	YGO1,PYGO2,RGS3,SEMA6A,SFRP4,SOST, TMEM47			Organismal Development]
7	ACP2,AHR,B4GAT1,CPM,CPSF6,DHRS9,EBF1,EFNB3,ERBB2,EXT2,FCHO2,FUT1,HECW2,HS3ST1,Igh(family),ITGB1,LMBRD2,MED1,NANOG,NUDT21,PHACTR2,PPARGC1B,S100A6,SCARA3,SEL1L3,SEMA7A,SLC43A3,SLC7A8,SLCO4A1,SMARCA4,SYVN1,TMEM106B,TPM4,TSPAN13,TUSC3	17	15	[Embryonic Development, Organ Development, Organismal Development]
8	APH1B,ATG14,BECN1,CERS6,CLSPN,CPEB3,DUT,E2F1,ERK1/2,ESCO2,ESYT1,GTPBP4,HERC2,ISCU,let7,MCM2,NAP1L1,NRBF2,OR51E1,PABPC4,PCSK5,PCSK7,PIK3R4,PSAT1,RPTOR,SNRPC,TAGLN2,THAP12,TP53,ULK2,UVRAG,VEGFD,VRK2,ZFYVE1,ZNF512B	14	13	[Carbohydrate Metabolism, Lipid Metabolism, Small Molecule Biochemistry]
9	ANGEL1,ANO6,EIF4E,EIF4EBP2,FLVCR1,HILPDA,HOXA5,HOXB5,IPO7,MXD1,MXRA5,MYC,Nc2,NELL2,NFIB,NMNAT1,NPM1,NUP50,NUP98DDX10,NUPR1,PARP1,PEG10,PLOD1,PLXND1,RPRD1B,SNHG17,SUPT5H,TCAF2,TEP1,USP36,VEGFA,YTHDC1,ZBTB34,ZFP36L1,ZNF521	14	13	[Embryonic Development, Organismal Development, Skeletal and Muscular System Development and Function]
10	ALPK3,APPL1,ARID1A,ARID4A,CEACAM6,CELSR2,CITED1,CLIC3,ESR1,FAM13C,FGFBP1,GOLM1,GPAM,GREB1,H4C3,HDAC1,HECTD1,KRT16,KRT4,KRT6A,KRT6B,MIER1,Mta,PDZK1,PIN1,PKNOX2,PRXL2A,PTGFRN,RNF181,SAP30,SLC2A4,SLC7A2,SNX24,TFF2,TOP2B	11	11	[Dermatological Diseases and Conditions, Developmental Disorder, Hereditary Disorder]

Table S2: List of top 16 hub genes with their respective interaction scores generated by the MCC method.

Gene	Score
<i>HIF1A</i>	75187
<i>CDH1</i>	74301
<i>CD44</i>	74210
<i>EGFR</i>	73498
<i>CCND1</i>	73068
<i>JAG1</i>	35528
<i>CD34</i>	32902
<i>FLT1</i>	25682
<i>PDGFRB</i>	22019
<i>GJA1</i>	16607
<i>ETS1</i>	15977
<i>STAT1</i>	15975
<i>ABCG2</i>	15843
<i>HNF4A</i>	15369
<i>TJP1</i>	15262
<i>LOX</i>	11123
<i>PDGFRB</i>	22019

Table S3: Primer sequences of miRNAs and genes.

miRNA	Primer Sequence
miR-140-5p	F 5'-GAGTGTCACTGGTTTTACCCT-3' R 5'GCAGGGTCCGAGGTATTC-3'
miR-143-5p	F 5'-GGGACAGACACCCGTTTTGA-3' R 5' GTGTTGCCCACGGTAATGCT-3'
miR-145-5p	F 5'-CAGAGTGCGTGTCTGGAGT-3' R 5'-AGGTCCAGTTTTCCCAGG-3'
miR-30a-5p	F 5'-GGGCCTGTAAACATCCTCG-3' R 5'-GAATACCTCGGACCCTGC-3'
miR-423-5p	F 5'-TTGGAGTAGGTCATTGGGTGG-3' R 5'-CCAAGACATGGAGGAGCCAT-3'
let-7i-5p	F 5'-TGAGGTAGTAGTTTGTGCTGTT-3' R 5'-GCCAGCACAGAATTAATACGAC-3'
miR-21-5p	F 5'-TTTTGTTTTGCTTGGGAGGA-3' R 5'-AGCAGACAGTCAGGCAGGAT-3'
U6	F 5'-CTCGCTTCGGCAGCACA-3' R 5'-AACGCTTCACGAATTTGCGT-3'

Gene	Primer Sequence
E-Cadherin	F 5'-ATTCTGATTCTGCTGCTCTTG-3' R 5'-AGTCCTGGTCCTCTTCTCC-3'
N-Cadherin	F 5'-CCACGCCGAGCCCCAGTATC-3' R 5'-CCCCCAGTCGTTCAAGTAATCA-3'

β -Actin	F 5'-CATGTACGTTGCTATCCAGGC-3' R 5'-CTCCTTAATGTCACGCACGAT-3'
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