

Table S1. Bacterial Strains

Strain	Relevant characteristics	Reference or source
<i>P. gingivalis</i>		
33277	Type strain	ATCC
381	Common laboratory strain	ATCC
W83	Common laboratory strain	ATCC
A7A1-28	Common laboratory strain	[1]
MP4-504	Low passage clinical isolate	[2]
$\Delta$ fimA	Isogenic mutant of 33277 lacking major fimbrial protein FimA	[3]
$\Delta$ mfa1	Isogenic mutant of 33277 lacking minor fimbrial protein Mfa1	[4]
$\Delta$ php1 $\Delta$ ltp1	Isogenic mutant of 33277 lacking the two major tyrosine phosphatases, Php1 and Ltp1	[5]
$\Delta$ serB	Isogenic mutant of 33277 lacking the serine phosphatase SerB	[6]
$\Delta$ porK	Isogenic mutant of 33277 lacking PorK and thus the T9SS is non-functional	Lab collection
$\Delta$ rgpA/B	Isogenic mutant of 33277 lacking the arginine gingipains RgpA and RgpB	[7]
$\Delta$ kgp	Isogenic mutant of 33277 lacking the lysine gingipain Kgp	[7]
$\Delta$ kgp $\Delta$ rgpA/B	Isogenic mutant of 33277 lacking the lysine gingipain Kgp and the arginine gingipains RgpA and RgpB	[7]
<i>S. gordonii</i>		
DL1	Common laboratory strain	Lab collection
$\Delta$ spxB	Isogenic mutant of DL1 lacking pyruvate oxidase and deficient in production of hydrogen peroxide	[8]
C $\Delta$ spxB	$\Delta$ spxB complemented with the wild type <i>spxB</i> allele in trans	[8]
$\Delta$ sspA/B	Isogenic mutant of DL1 lacking the SspA/B adhesins	[8]
$\Delta$ cbe	Isogenic mutant of DL1 lacking chorismite binding enzyme and unable to produce pABA	[9]
<i>S. mutans</i> KPSK2	Common laboratory strain	Lab collection
<i>S. oralis</i> 10557	Common laboratory strain	Lab collection
<i>S. sanguinis</i> 10556	Common laboratory strain	Lab collection
<i>S. constellatus</i> 27823	Common laboratory strain	ATCC
<i>T. denticola</i> 35405	Type strain	ATCC
<i>F. nucleatum</i> 25586	Type strain	ATCC
<i>F. alocis</i> 35896	Type strain	ATCC

Table S2. Eukaryotic Cells

Cell name	Relevant characteristics	Reference or source
TIGK	Telomerase immortalized gingival epithelial cells	[10]
OKF6/TERT2	Telomerase immortalized oral mucosa cells	[11]
SCC9	Derived from tongue squamous cell carcinoma	ATCC
ESCC9706	Derived from esophageal squamous cell carcinoma	[12]

Table S3. Antibodies and Reagents

Item	Supplier
OLFM4, Activated Notch1, and GAPDH antibodies	Abcam, Cambridge, MA
Phalloidin- Texas Red, Alexa Fluor 488, DAPI, and OLFM4 ELISA	ThermoFisher, Waltham, MA
OLFM4, Notch1, Notch2, Notch3, Notch4, Jag1, Jag2, DLL1, DLL3, DLL4, ZEB2, $\beta$ -catenin, ADAM10, ADAM17, and NLK trilencer-27 siRNA	Origene, Rockville, MD
TLCK, FH535, LY-374973, and L-BAPNA	Sigma-Aldrich, St Louis. MO
TAPI-2	Tocris, Minneapolis, MN

## References

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2. Lamont RJ, Chan A, Belton CM, Izutsu KT, Vasel D, Weinberg A. *Porphyromonas gingivalis* invasion of gingival epithelial cells. *Infect Immun* 1995; **63**: 3878-3885.
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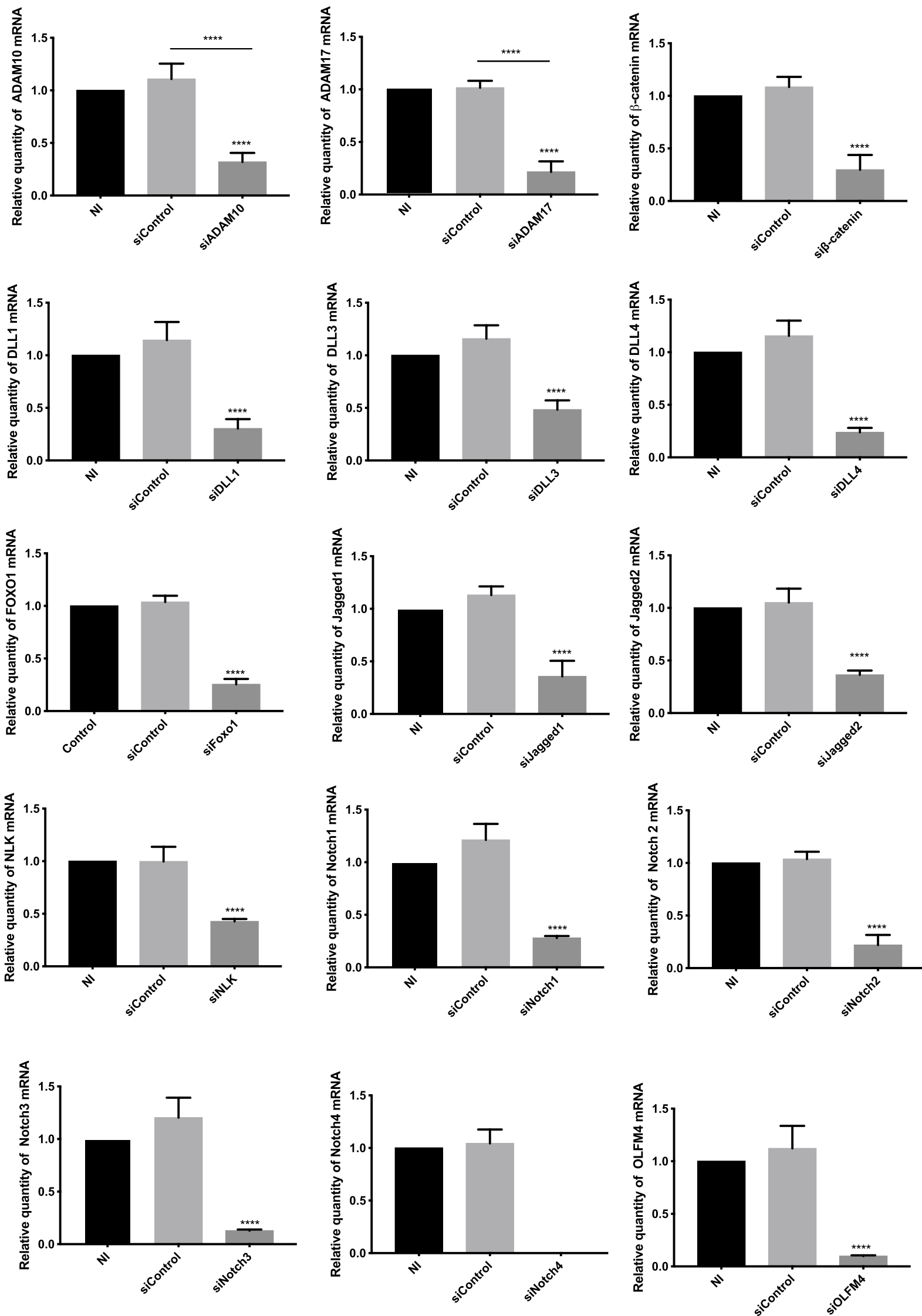
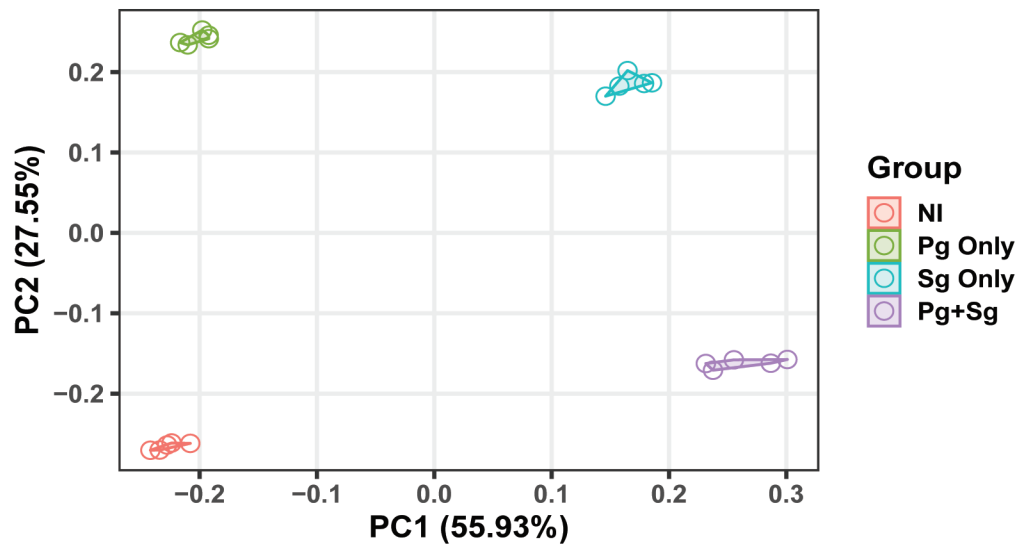
**A**

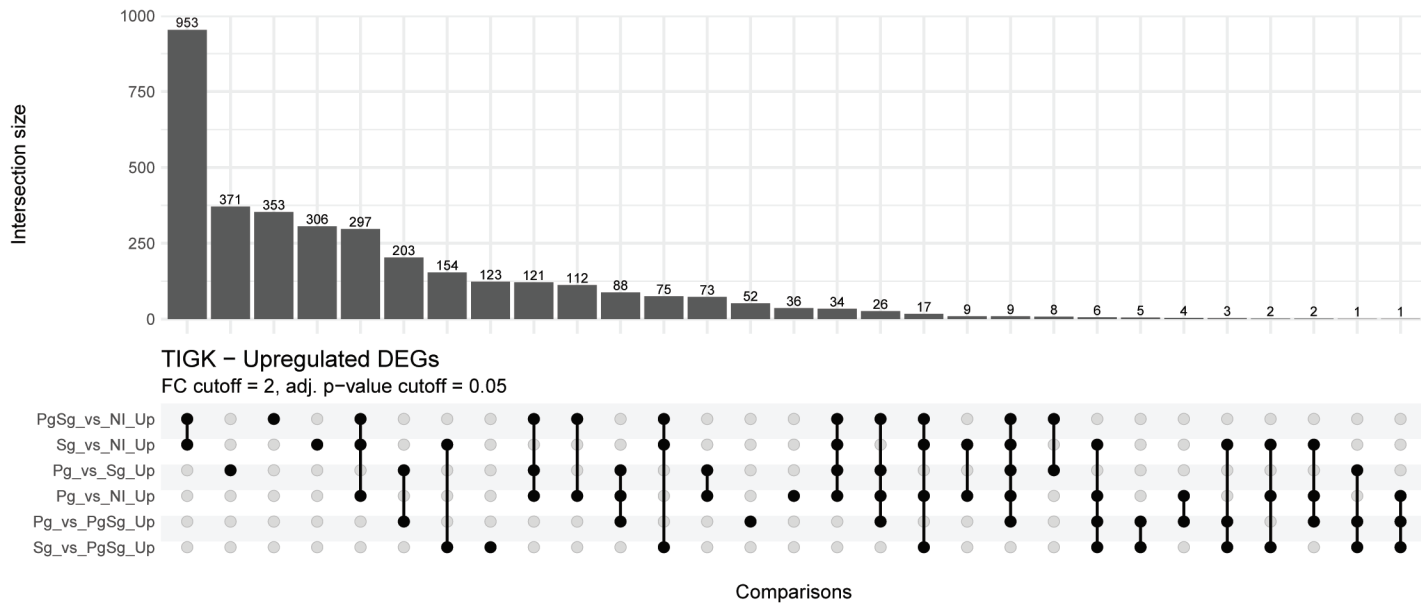
Figure S1

A

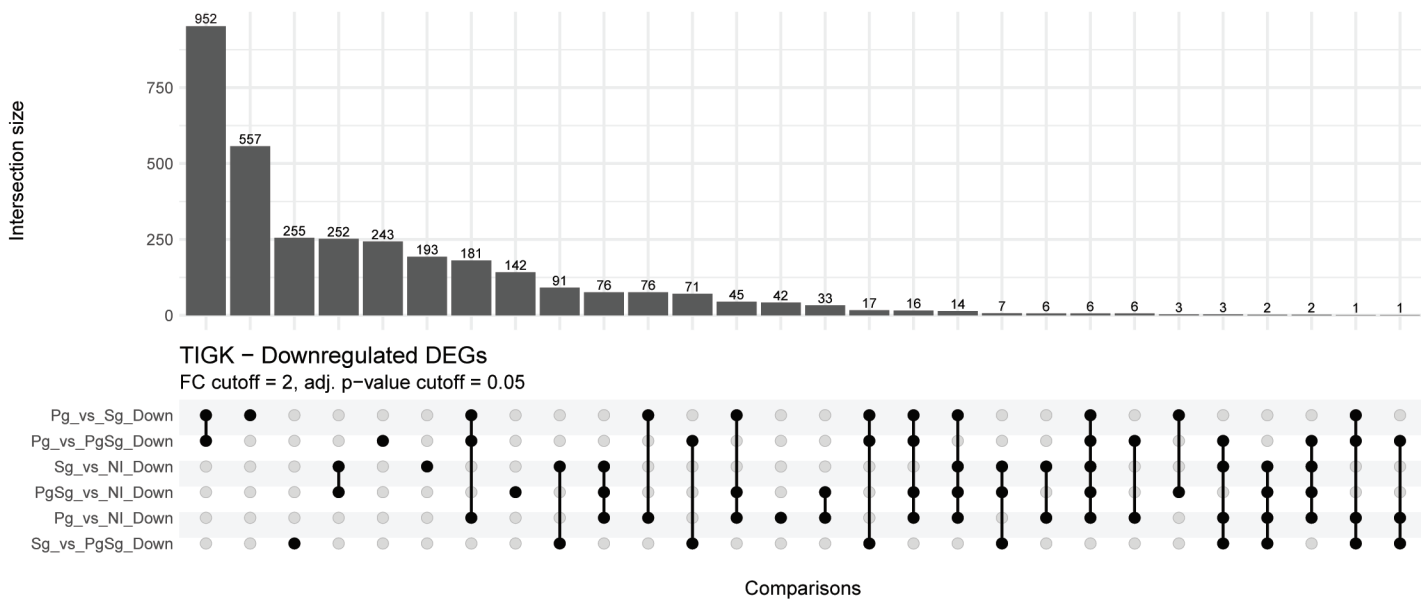
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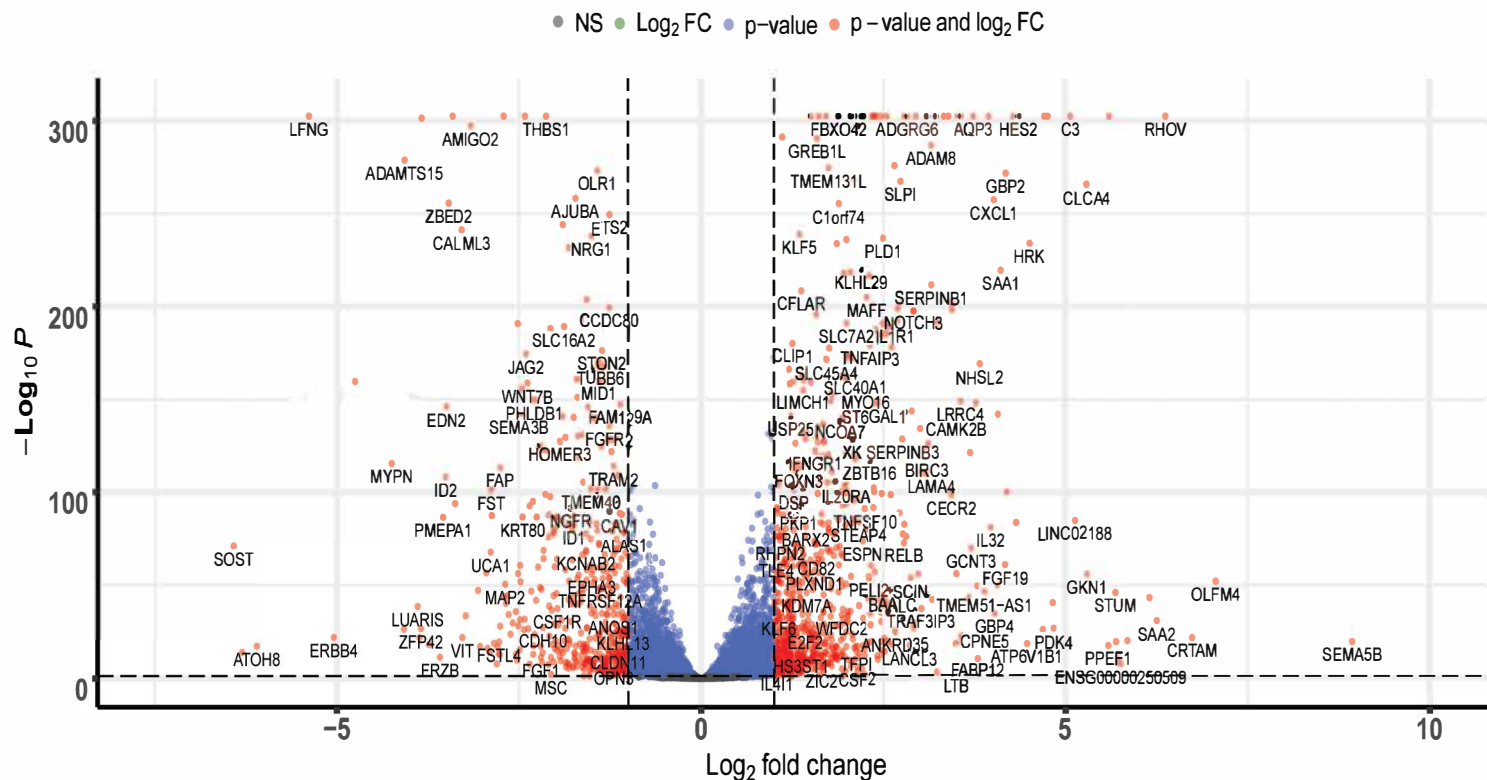
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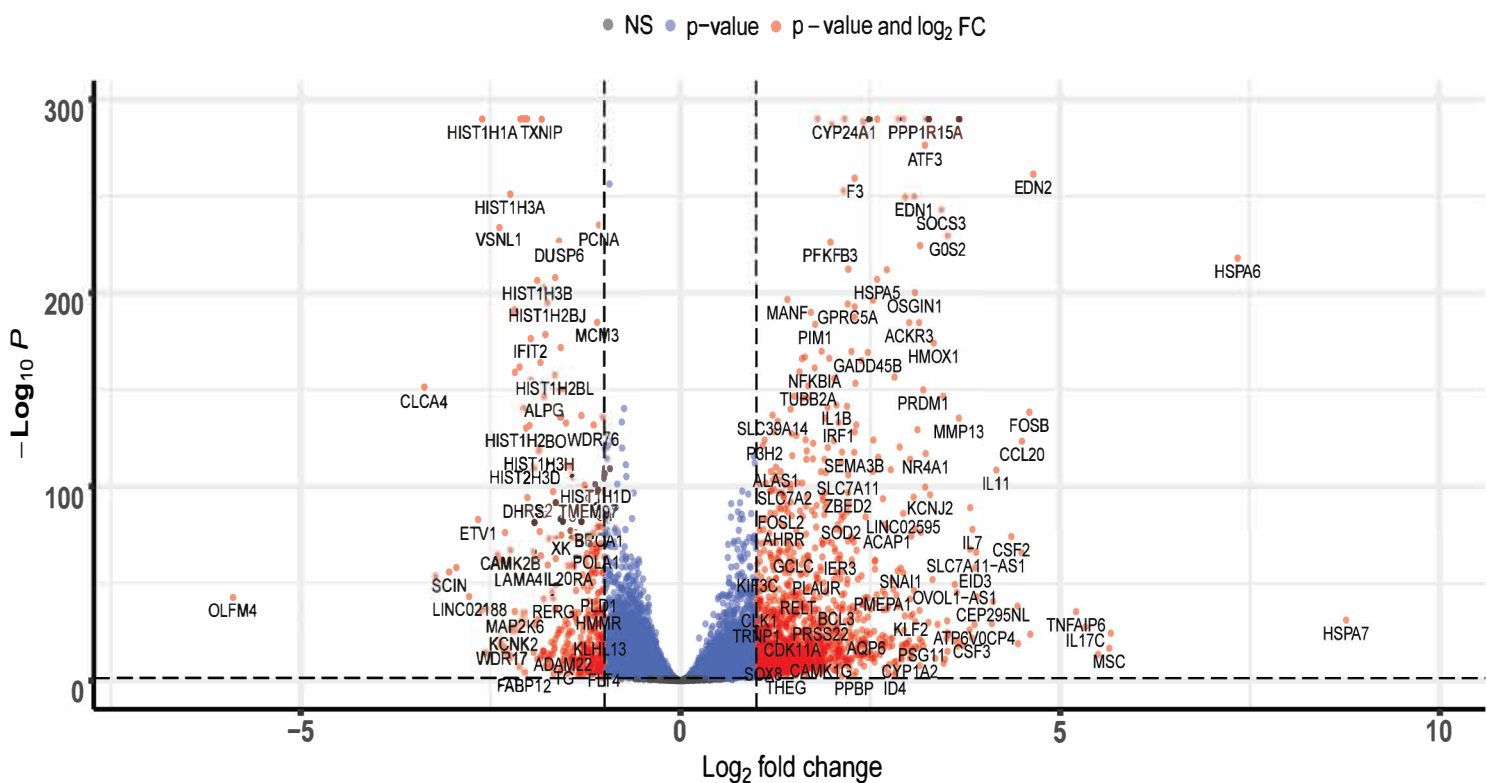
C



D

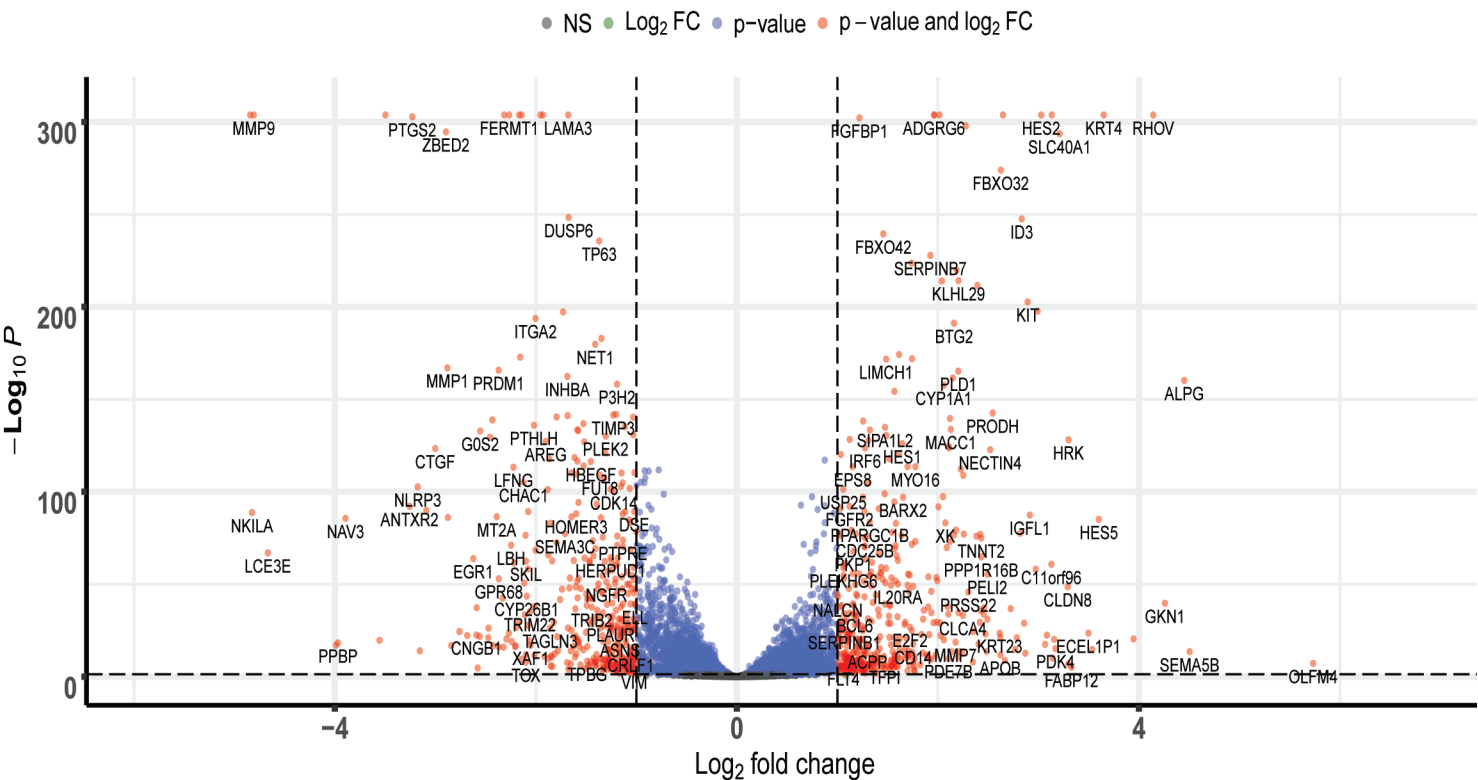
**Pg vs. NI**Log<sub>2</sub>FC cutoff = 1, adj. p-value cutoff = 0.05

E

**Pg+Sg vs Pg**Log<sub>2</sub>FC cutoff = 1, adj. p-value cutoff = 0.05

F

## Pg+Sg vs Sg

Log<sub>2</sub>FC cutoff = 1, adj. p-value cutoff = 0.05

G

## Pg vs Sg

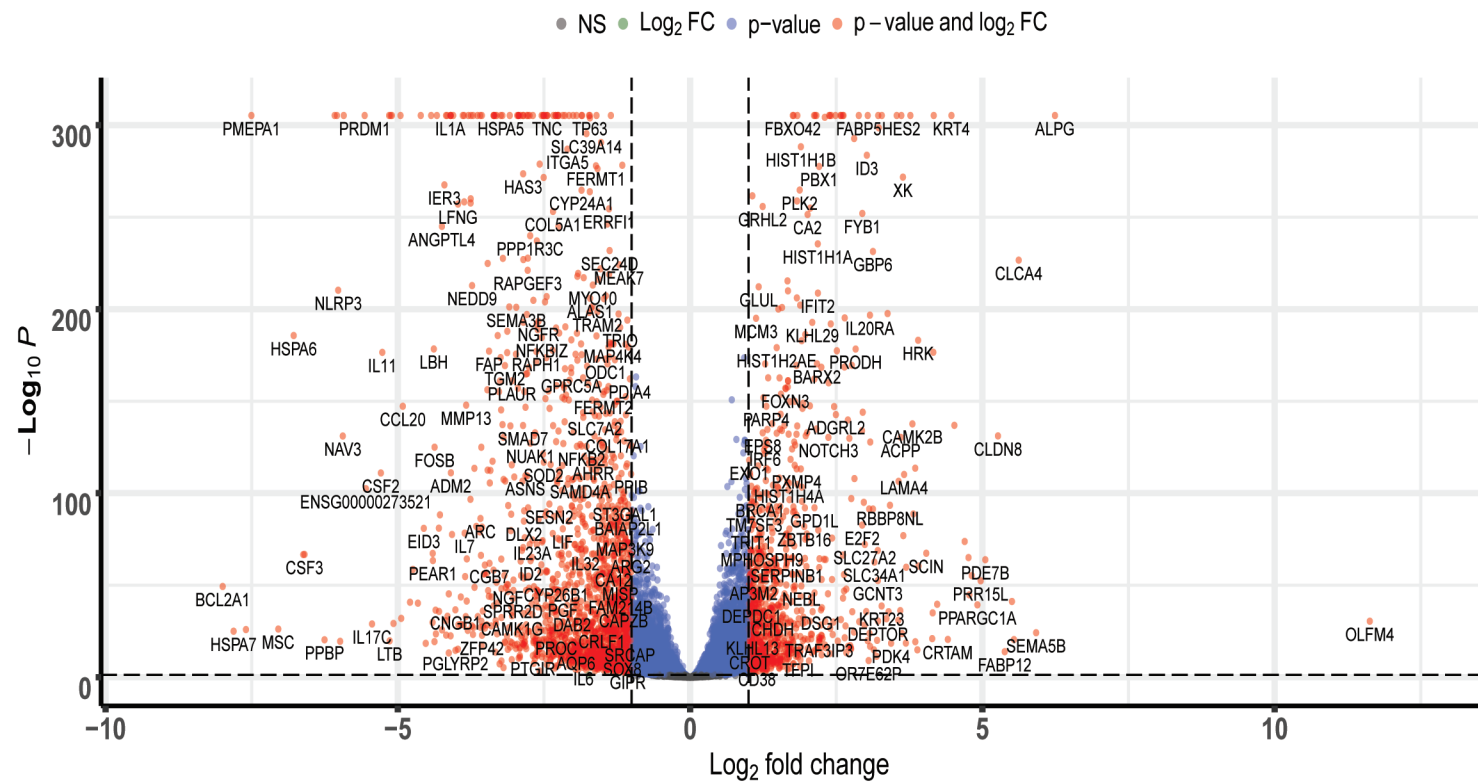
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Figure S2

Total = 14607 input genes

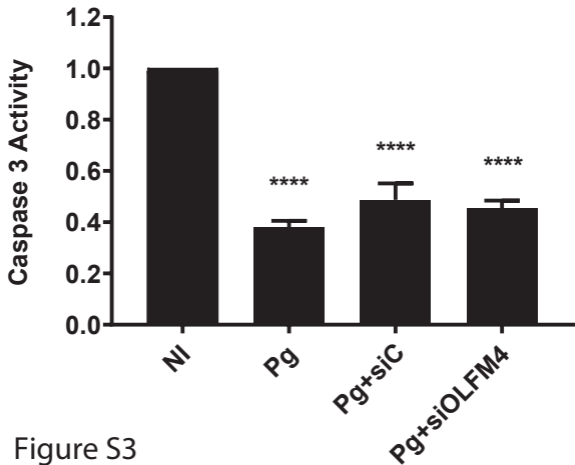


Figure S3



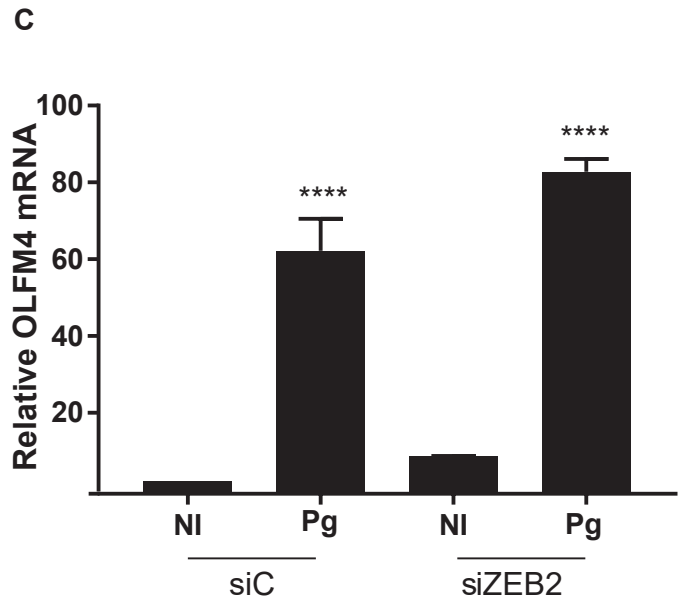
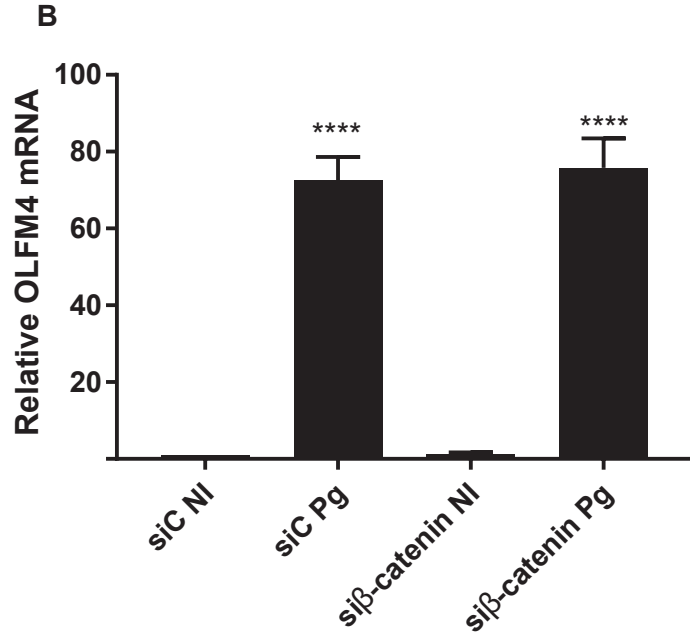
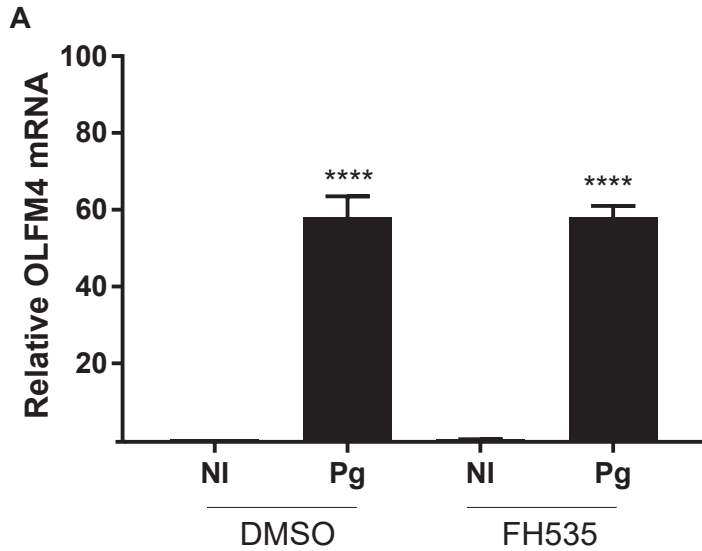
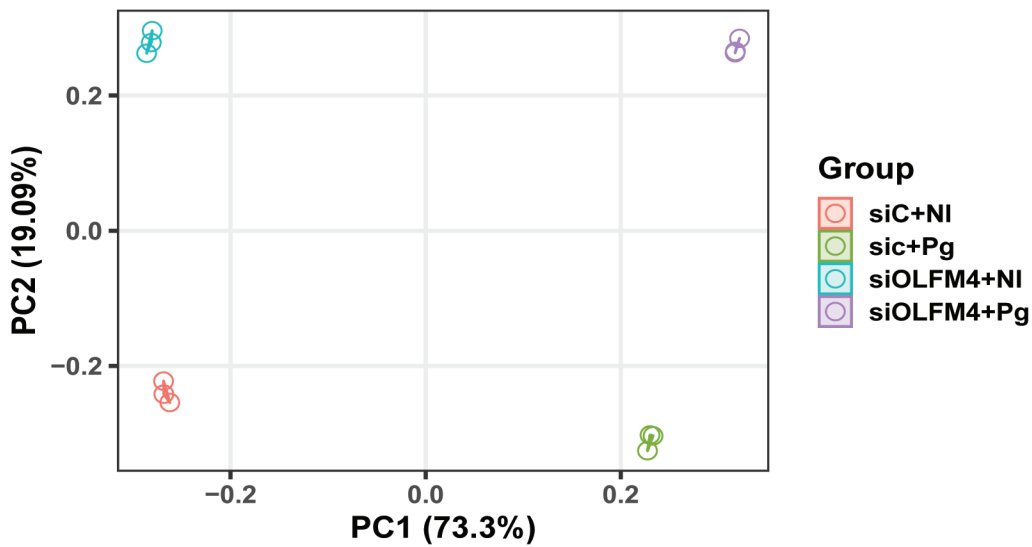


Figure S4

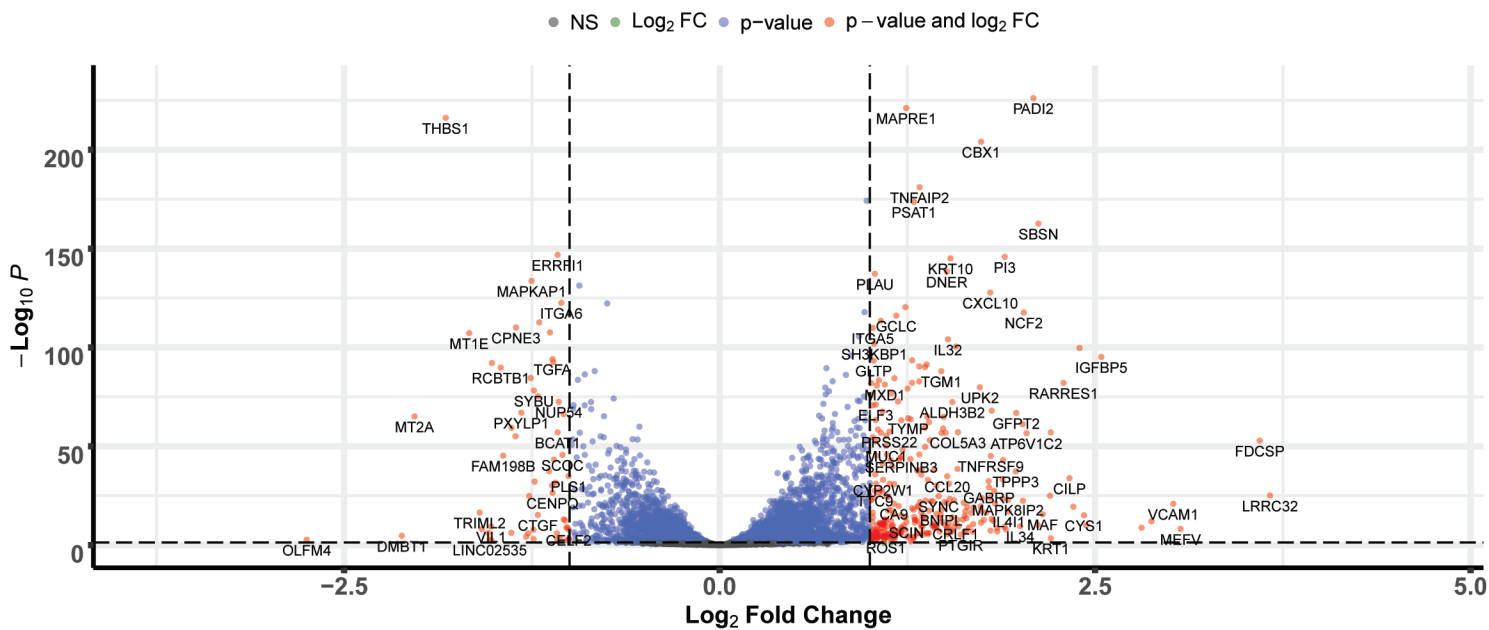
A

## PCA

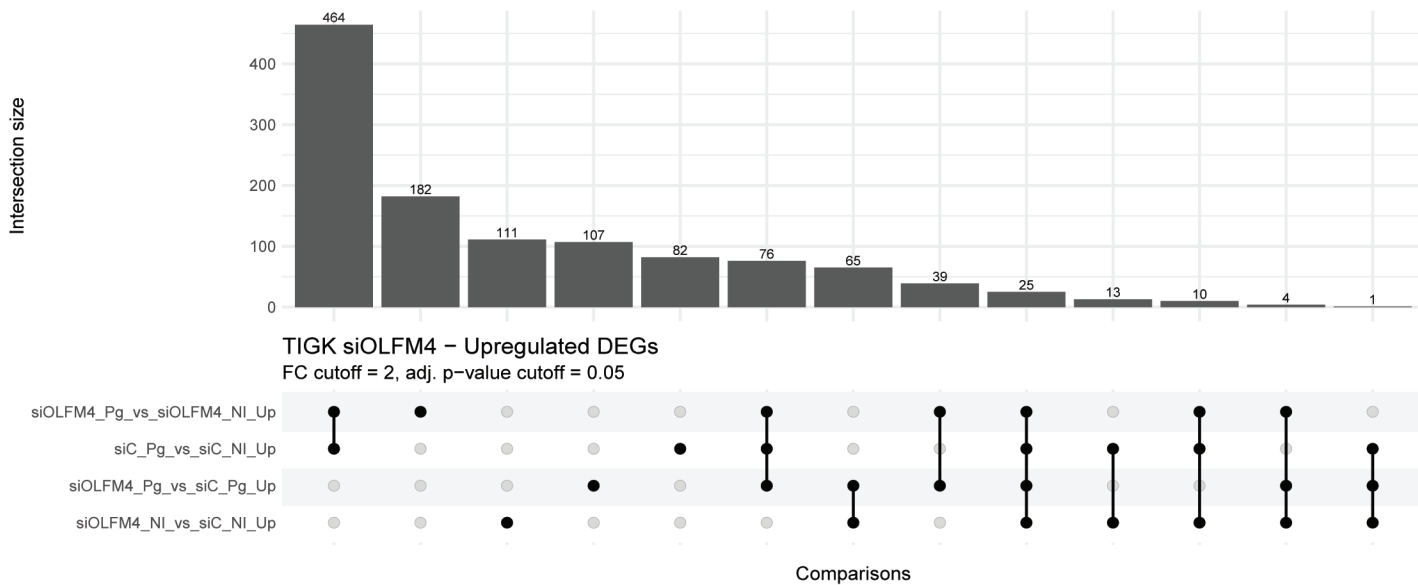


B

## siOLFM4+Pg vs. siC+Pg

Log<sub>2</sub>FC cutoff = 1, adj. p-value cutoff = 0.05

C



D

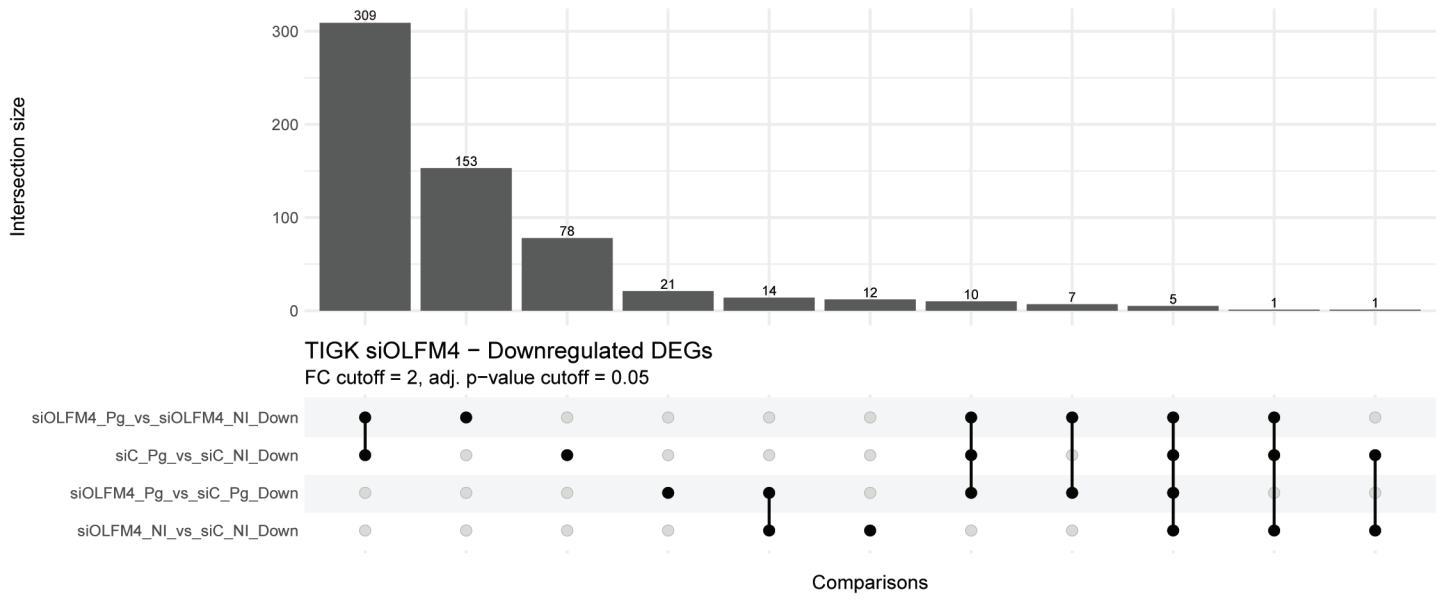


Figure S5

## Supplementary Figure Legends

**Figure S1.** Confirmation of siRNA knockdown of target genes as indicated by qRT-PCR. \*\*\*\* $p < 0.001$  compared to siControl.

**Figure S2. Transcriptomic responses of TIGKs to challenge with *P. gingivalis* and *S. gordonii*.** TIGK cells were challenged with *P. gingivalis* (Pg) MOI 100, *S. gordonii* (Sg) MOI 100, Pg MOI 50 in combination with Sg MOI 50, or noninfected (NI). A) Principal Component Analysis (PCA) of RNA-Seq. Each biological replicate for infected and noninfected (NI) is shown on the first two components of the principal component analysis. B-C) UpSet charts of differentially expressed genes (DEGs) in common amongst treatment groups using the ComplexUpSet R package. D-G) Volcano plots of differentially expressed transcripts amongst treatment groups. X-axis shows log-fold change between the two conditions with positive values showing upregulation and negative values showing downregulation. Y-axis denotes  $p$  values for corresponding genes. Significantly differentially expressed genes are shown in red ( $p < 0.05$ , log<sub>2</sub> fold change  $> 1$ ), as determined using the DESeq package in R.

**Figure S3. Suppression of apoptosis in TIGKs by *P. gingivalis* is independent of OLFM4.** TIGKs were transiently transfected with siRNA to OLFM4 or scrambled siRNA (siC), challenged with *P. gingivalis* (Pg), and apoptosis induced with camptothecin. Caspase 3 activity is presented relative to uninfected (NI) control. Data are means with SD and representative of 3 biological replicates. \*\*\*\*  $p < 0.001$ .

**Figure S4. Wnt/ $\beta$ -catenin and ZEB2 are not required for activation of OLFM4 by *P. gingivalis*.** qRT-PCR of OLFM4 transcripts. A) TIGKs were pretreated with FH525 or DMSO and challenged with *P. gingivalis* (Pg). B) TIGK cells were transiently transfected with siRNA to  $\beta$ -catenin or scrambled siRNA (siC) and challenged with *P. gingivalis* (Pg). C) TIGK cells were transiently transfected with siRNA to ZEB2 or scrambled siRNA (siC) and challenged with *P. gingivalis* (Pg).

OLFM4 mRNA levels are expressed relative to noninfected (NI) controls. Data are means with SEM. \*\*\*\* $p < 0.001$  compared to uninfected (NI).

**Figure S5. OLFM4 controls TIGK inflammatory responses.** TIGKs were transiently transfected with siRNA to OLFM4 or scrambled siRNA (siC), and challenged with *P. gingivalis* (Pg) or left uninfected (NI). A) PCA plot of RNA-Seq analysis of each group. B) Volcano plots of differentially expressed transcripts dependent on reduction of OLFM4 in the Pg infected group. X-axis shows log-fold change between the two conditions with positive values showing upregulation and negative values showing downregulation. Y-axis denotes  $p$  values for corresponding genes. Significantly differentially expressed genes are shown in red ( $p < 0.05$ , log<sub>2</sub> fold change  $> 1$ ). C- D) UpSet charts of DEGs in common amongst treatment groups.