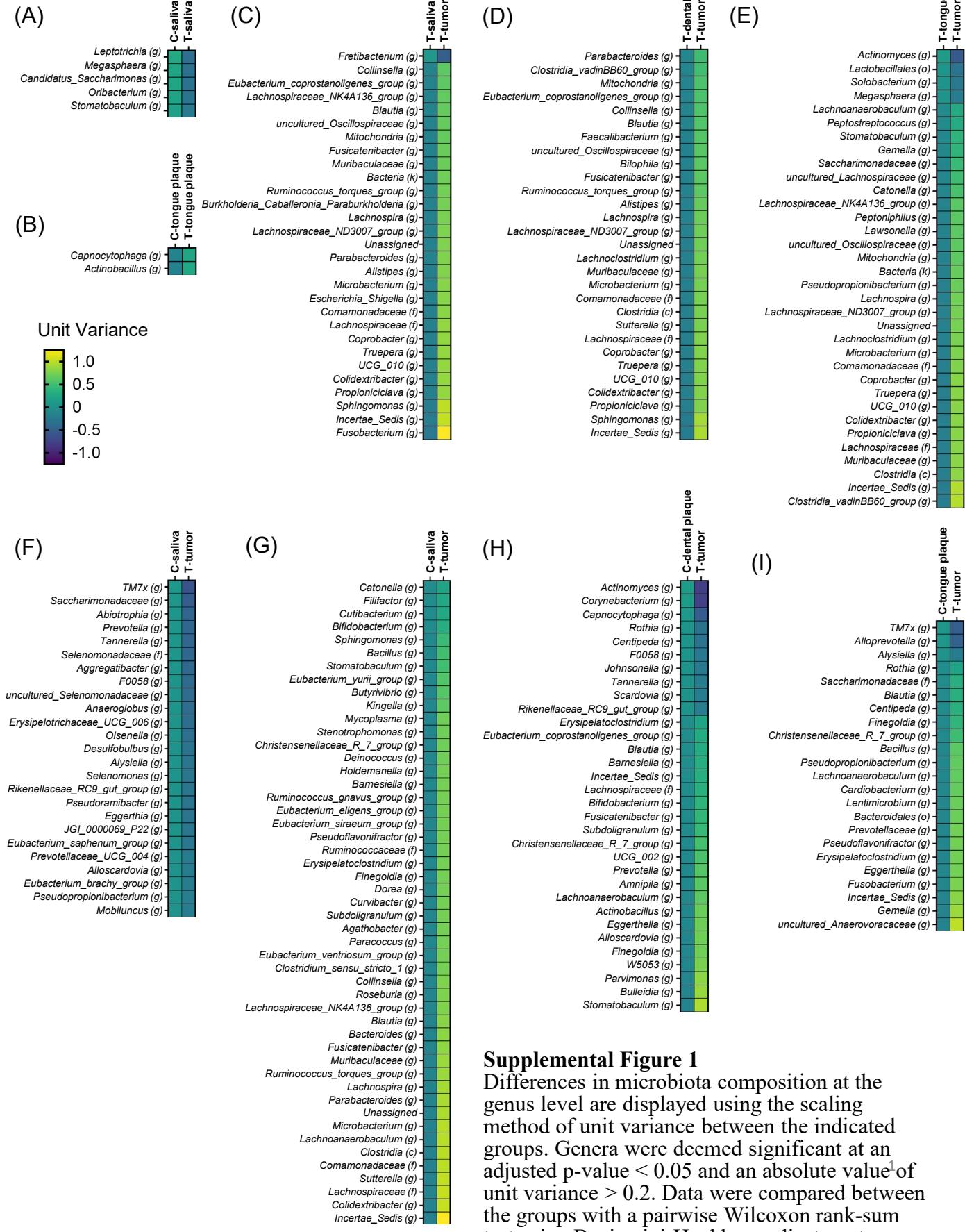


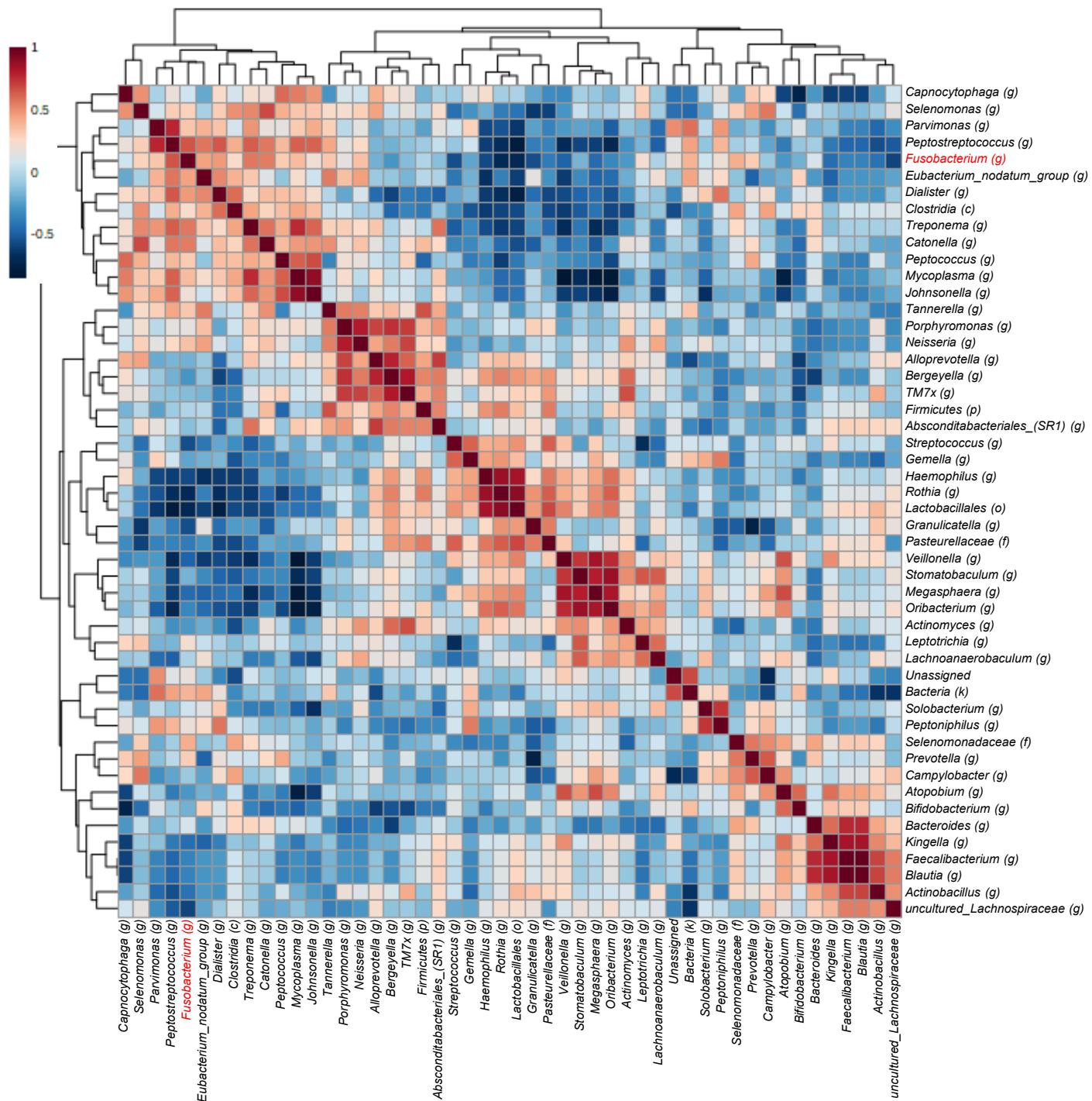
# Supplemental Figure. S1



## Supplemental Figure 1

Differences in microbiota composition at the genus level are displayed using the scaling method of unit variance between the indicated groups. Genera were deemed significant at an adjusted p-value < 0.05 and an absolute value<sup>1</sup> of unit variance > 0.2. Data were compared between the groups with a pairwise Wilcoxon rank-sum test using Benjamini-Hochberg adjustment.

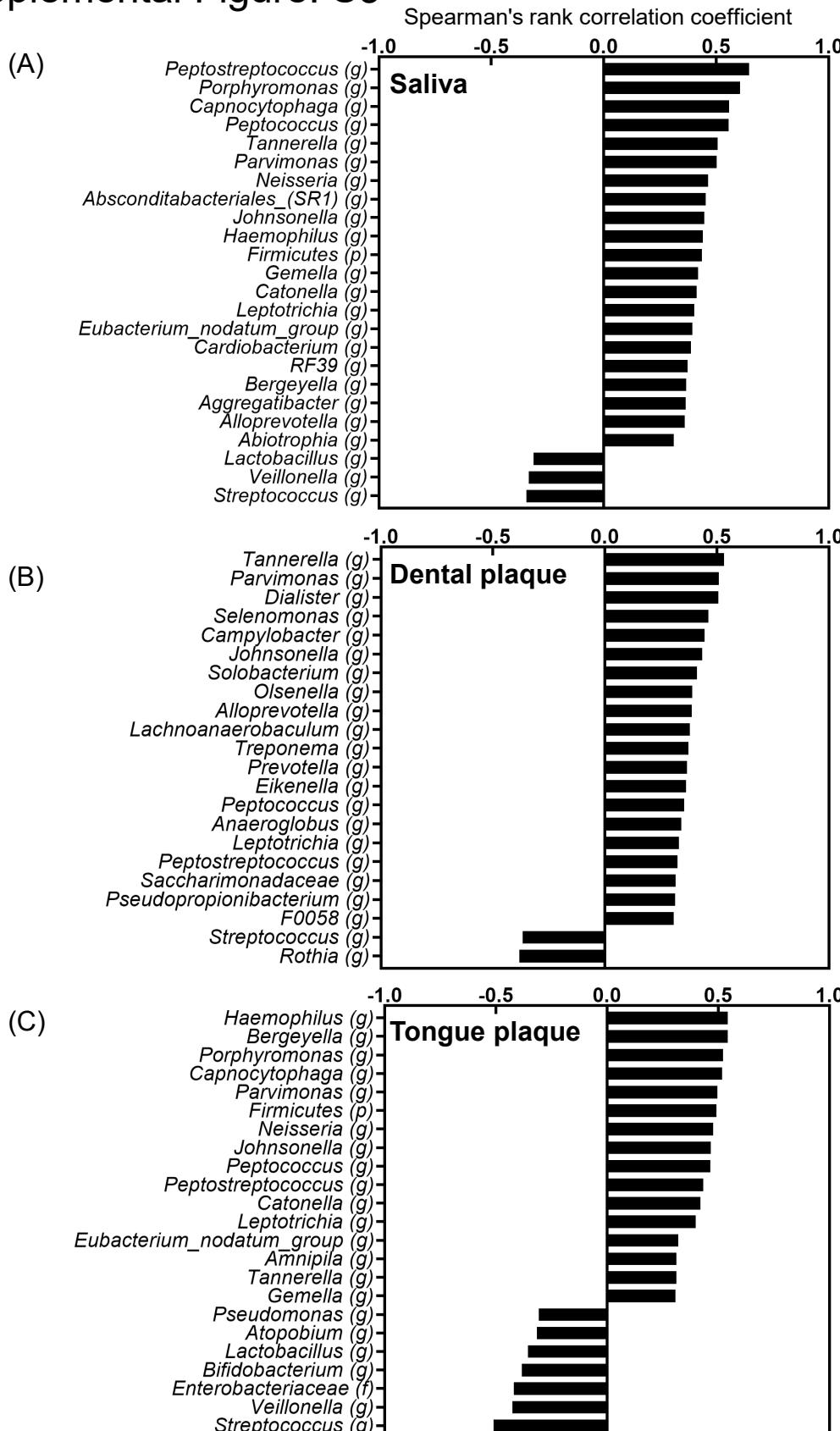
# Supplemental Figure. S2



## Supplemental Figure 2

Co-occurrence analysis of the top 50 bacterial genera in tumor tissues from oral cancer patients is depicted using Spearman's rank correlation coefficient in a heat map.

# Supplemental Figure. S3



## Supplemental Figure 3

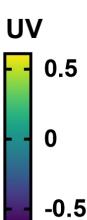
Correlation between the abundance of *Fusobacterium* and other bacterial genera in saliva (A), dental plaque (B), and tongue plaque (C) between the control and oral cancer patient groups is showcased using Spearman's rank correlation coefficient in bar plots.

# Supplemental Figure. S4

(A) T<sub>saliva</sub> T<sub>tumor</sub>  
Pathway Class

## MetaCyc Pathway (*F. nucleatum*)

UV	Pathway Class	Description
-0.5	Secondary Metabolites Biosynthesis	NONMEVIPP-PWY: methylenethitol phosphate pathway I
-0.5	Nucleosides and Nucleotides Biosynthesis	PWY-7560: methylenethitol phosphate pathway II
-0.5	Glycolysis	PWY-7221: guanosine ribonucleotides de novo biosynthesis
-0.5	Fermentation	PWY-6609: adenine and adenosine salvage III
-0.5	Degradation/Utilization/Assimilation - Other	PWY-6700: queuosine biosynthesis I (de novo)
-0.5	Cofactors, Prosthetic Groups, Electron Carriers Biosynthesis	PWY-6124: inosine-5'-phosphate biosynthesis II
-0.5	Cell Structures Biosynthesis	PWY-6123: inosine-5'-phosphate biosynthesis I
-0.5	Carbohydrates Degradation	PWY-6122: 5-aminoimidazole ribonucleotide biosynthesis II
-0.5	Aromatic Compounds Biosynthesis	PWY-6277: superpathway of 5-aminoimidazole ribonucleotide biosynthesis
-0.5	Amino Acids Degradation	PWY-6121: 5-aminoimidazole ribonucleotide biosynthesis I
-0.5	Amines and Polyamines Degradation Superpathways	PWY-5686: UMP biosynthesis I
-0.5	Alcohols Degradation	ANAGLYCOLYSIS-PWY: glycolysis III (from glucose)
-0.5	Secondary Metabolites Biosynthesis	PWY-7111: pyruvate fermentation to isobutanol (engineered)
-0.5	Secondary Metabolites Biosynthesis	P41-PWY: pyruvate fermentation to acetate and (S)-lactate I
-0.5	Secondary Metabolites Biosynthesis	PWY-5100: pyruvate fermentation to acetate and lactate II
-0.5	Secondary Metabolites Biosynthesis	PWY-7663: gondate biosynthesis (anaerobic)
-0.5	Secondary Metabolites Biosynthesis	PWY-5981: CDP-diacylglycerol biosynthesis III
-0.5	Secondary Metabolites Biosynthesis	P161-PWY: acetylene degradation (anaerobic)
-0.5	Coenzyme A Biosynthesis	COA-PWY: coenzyme A biosynthesis I (prokaryotic)
-0.5	Coenzyme A Biosynthesis	PWY-7357: thiamine phosphate formation from pyritiamine and oxythiamine (yeast)
-0.5	Coenzyme A Biosynthesis	PWY-5121: superpathway of geranylgeranyl diphosphate biosynthesis II (via MEP)
-0.5	Coenzyme A Biosynthesis	PWY-5188: tetrapyrrole biosynthesis I (from glutamate)
-0.5	Coenzyme A Biosynthesis	COA-PWY-1: superpathway of coenzyme A biosynthesis III (mammals)
-0.5	Peptidoglycan Biosynthesis	PEPTIDOGLYCANSYN-PWY: peptidoglycan biosynthesis I (meso-diaminopimelate containing)
-0.5	Peptidoglycan Biosynthesis	PWY-6387: UDP-N-acetylmuramoyl-pentapeptide biosynthesis I (meso-diaminopimelate containing)
-0.5	Peptidoglycan Biosynthesis	PWY-6386: UDP-N-acetylmuramoyl-pentapeptide biosynthesis II (lysine-containing)
-0.5	Peptidoglycan Biosynthesis	PWY-6385: peptidoglycan biosynthesis III (mycobacteria)
-0.5	O antigen building blocks Biosynthesis	OANTIGEN-PWY: O-antigen building blocks biosynthesis ( <i>E. coli</i> )
-0.5	GDP-mannose Biosynthesis	PWY-5659: GDP-mannose biosynthesis
-0.5	dTDP-Rhamnose Biosynthesis	DTDPRHAMNSYN-PWY: dTDP-β-L-rhamnose biosynthesis
-0.5	D-galactose Degradation	PWY-6317: D-galactose degradation I (Leloir pathway)
-0.5	Glycogen Biosynthesis	GLYCOGENSYNTH-PWY: glycogen biosynthesis I (from ADP-D-Glucose)
-0.5	Starch Biosynthesis	PWY-622: starch biosynthesis
-0.5	Glycogen Degradation	PWY-5941: glycogen degradation II
-0.5	Sucrose Biosynthesis	PWY-7238: sucrose biosynthesis II
-0.5	Chorismate Biosynthesis	ARO-PWY: chorismate biosynthesis I
-0.5	Chorismate Biosynthesis	PWY-6163: chorismate biosynthesis from 3-dehydroquinate
-0.5	L-histidine Degradation	PWY-5030: L-histidine degradation III
-0.5	L-histidine Degradation	HISDEG-PWY: L-histidine degradation I
-0.5	L-lysine Fermentation	P163-PWY: L-lysine fermentation to acetate and butanoate
-0.5	Branched-chain AA Synthesis	BRANCHED-CHAIN-AA-SYN-PWY: superpathway of branched chain amino acid biosynthesis
-0.5	Aromatic AA Biosynthesis	COMPLETE-ARO-PWY: superpathway of aromatic amino acid biosynthesis
-0.5	L-isoleucine Biosynthesis	ILEUSYN-PWY: L-isoleucine biosynthesis I (from threonine)
-0.5	L-isoleucine Biosynthesis	PWY-5103: L-isoleucine biosynthesis III
-0.5	S-adenosyl-L-methionine Salvage	PWY-6151: S-adenosyl-L-methionine salvage I
-0.5	Asparagine Biosynthesis	ASPASN-PWY: superpathway of L-aspartate and L-asparagine biosynthesis
-0.5	Glcmannan Biosynthesis	GLCMANNANAUT-PWY
-0.5	(S)-propane-1,2-diol Degradation	PWY-7013: (S)-propane-1,2-diol degradation

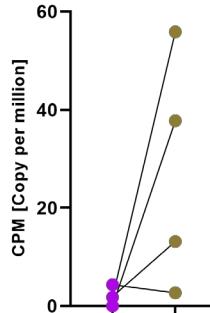


## Pathway Class

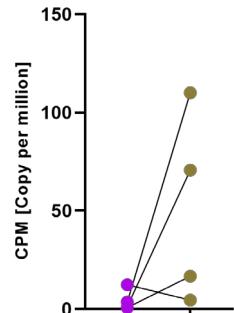
Secondary Metabolites Biosynthesis
Nucleosides and Nucleotides Biosynthesis
Glycolysis
Fermentation
Fatty Acid and Lipid Biosynthesis
Degradation/Utilization/Assimilation - Other
Cofactors, Prosthetic Groups, Electron Carriers Biosynthesis
Cell Structures Biosynthesis
Carbohydrates Degradation
Aromatic Compounds Biosynthesis
Amino Acids Degradation
Amino Acids Biosynthesis
Amines and Polyamines Degradation Superpathways
Alcohols Degradation

(B)

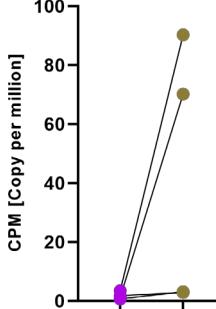
## GDP-mannose biosynthesis



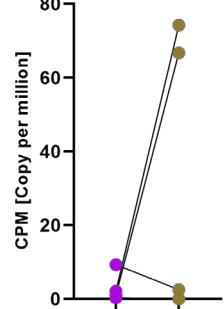
## D-galactose degradation I (Leloir pathway)



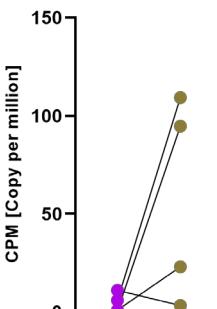
## Glycogen biosynthesis I (from ADP-D-Glucose)



## Starch biosynthesis



## dTDP-β-L-rhamnose biosynthesis



● T<sub>saliva</sub> ● T<sub>tumor</sub>

## Supplemental Figure 4

(A) All microbial pathways of *Fusobacterium nucleatum* associated with saliva and tumors from oral cancer patients were identified with the HUMAnN3 tool, analyzing microbial gene families. Pathway abundances are based on copies per million (CPM), and differences in CPM are displayed using the scaling method of unit variance between the groups. (B) Indicated pathway abundances of *F. nucleatum* in saliva and tumors from the same oral cancer patients are shown.

# Supplemental Figure. S5

## Fusobacterium nucleatum subsp. polymorphum strain KCOM 1260 (=ChDC F218) genome

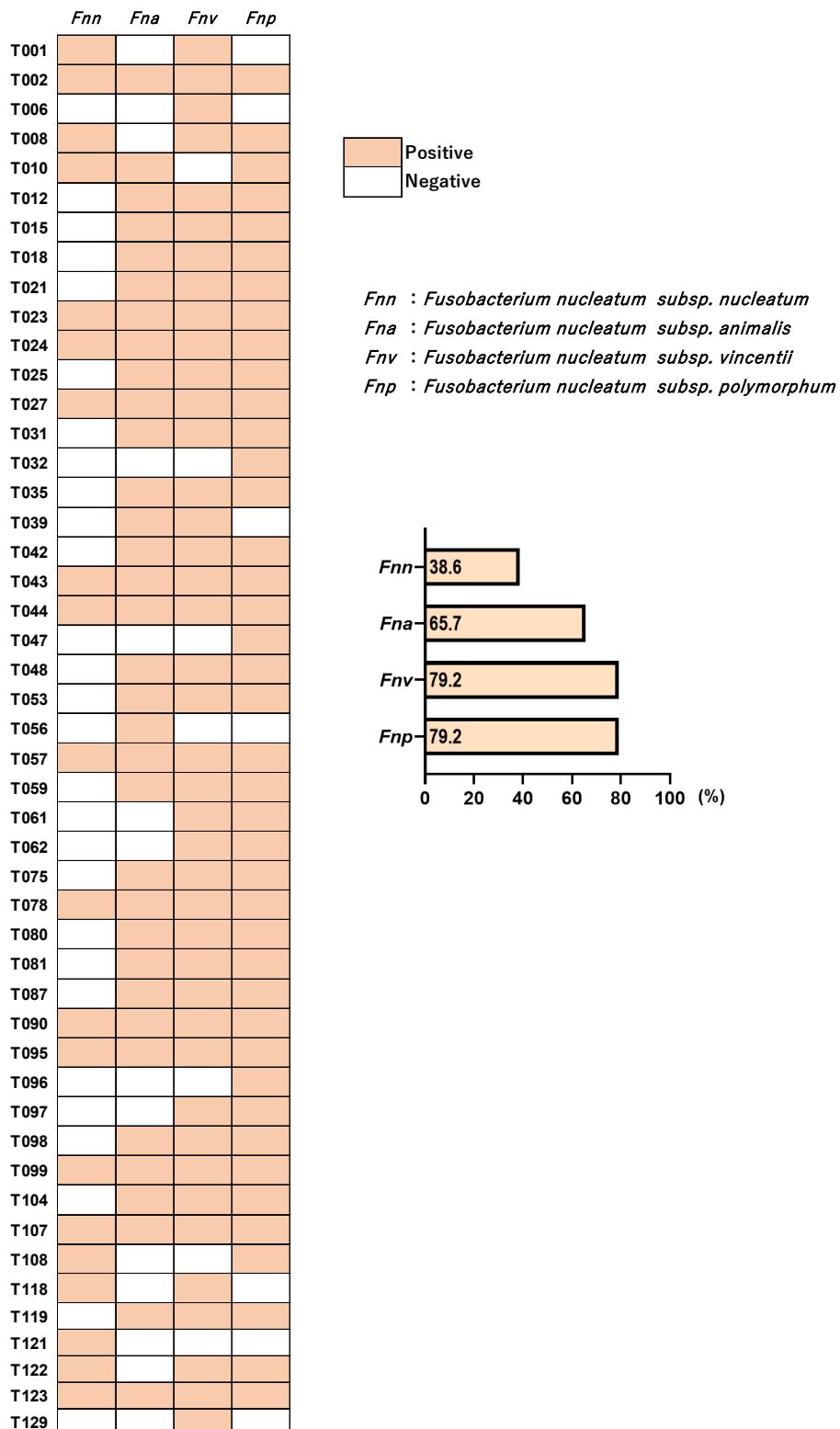
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Range 1: 1706311 to 1707158 <a href="#">GenBank</a> <a href="#">Graphics</a>					<a href="#">▼ Next Match</a>	<a href="#">▲ Previous Match</a>
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Sbjct 1707098	GAGAGGTAACGGCTCACCAAGGCATGATGGGTAGCCGGCTGAGAGGGTATCGGCCAC		1707039			
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Sbjct 1706319	ATGG-CTGTC 1706311					

## Supplemental Figure 5

Isolated *Fn* from oral cancer patient's saliva was 99% identical to *Fn polymorphum* by BLAST search.

# Supplemental Figure. S6



## Supplemental Figure 6

The existence of four major *Fn* subspecies in oral cancer patients' saliva is displayed. Orange highlighted squares show the existence of *Fn* subspecies as indicated.