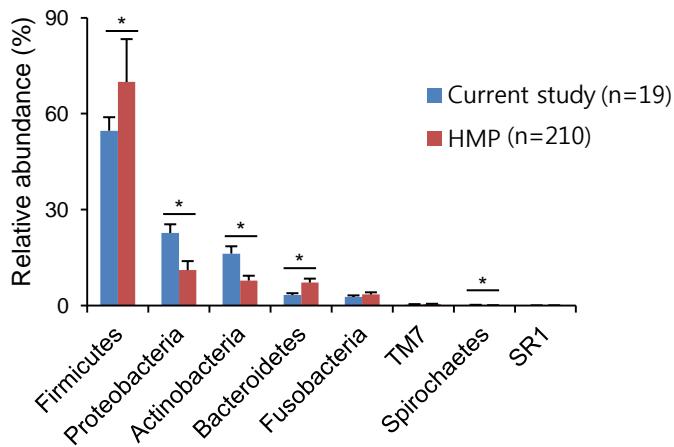
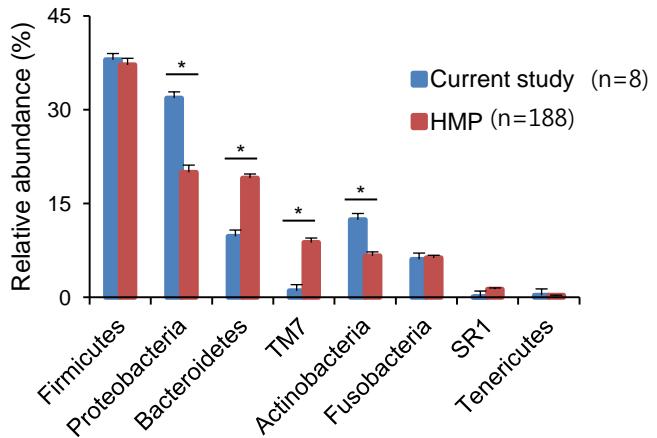


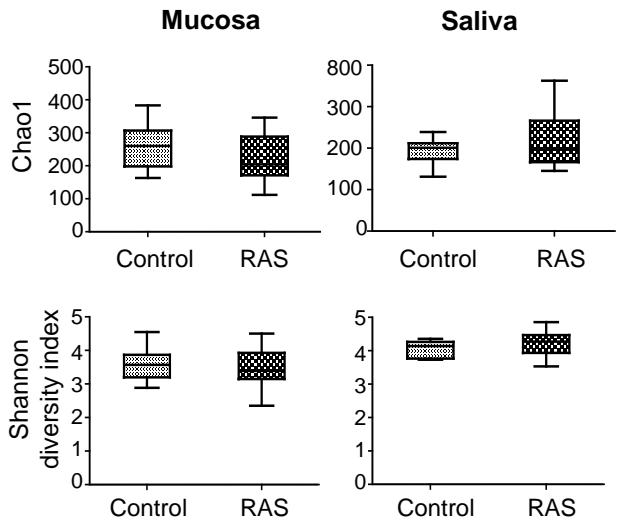
Figure S1

A**B**

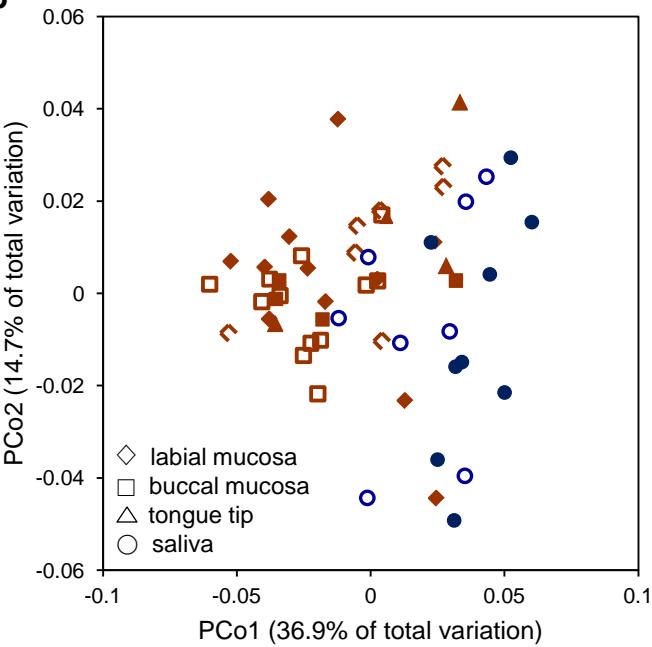
Dominant phyla observed in the mucosa (A) and saliva (B) of control subjects were compared with those published by Human Microbiome Project Consortium.

Figure S2

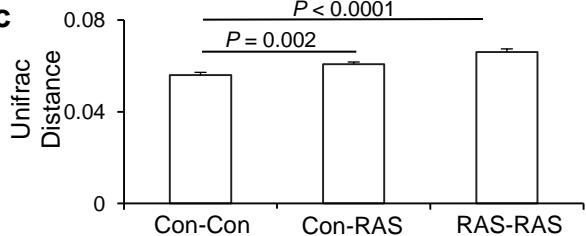
a



b



c



d

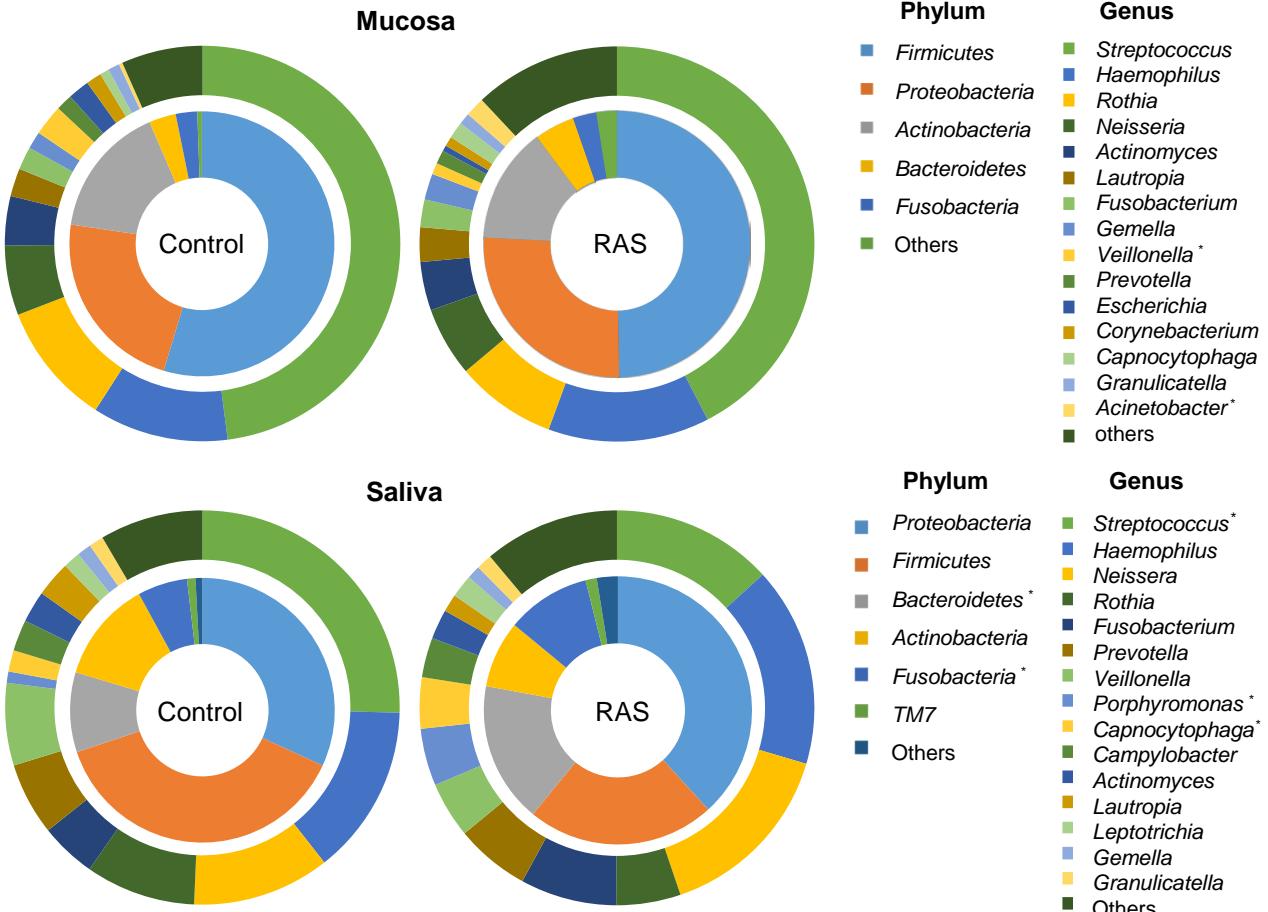
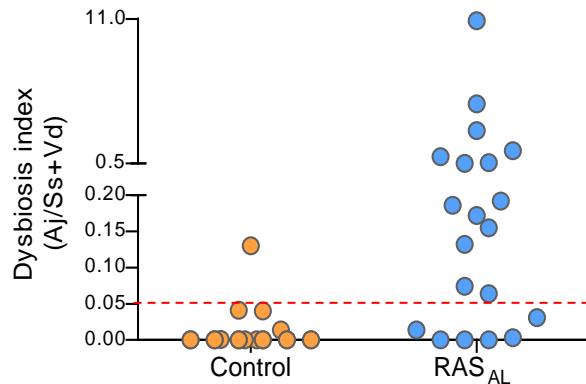


Figure S3



Dysbiosis index of RAS A logistic regression analysis of the mucosal microbiota using a forward method revealed that the abundance (per % increase) of *S. salivarius* was associated with a reduced RAS risk (odds ratio [OR] 0.691, 95% confidence interval [95% CI] 0.526-0.909, $P=0.008$). The analysis using a backward method revealed two species. The abundance of *V. dispar* was associated with a reduced RAS risk (OR 0.124, CI 95% 0.024-0.646, $P=0.013$), and the abundance of *A. johnsonii* was associated with an increased RAS risk (OR 7547, CI 95% 4.9-1.2E7, $P=0.017$). A dysbiosis index was defined as the relative abundance of *A. johnsonii* divided by the relative abundance of *S. salivarius* plus *V. dispar* in the mucosa.

Table. 1 . The demographic data of control subjects and RAS patients.

	Control subjects (n = 19)	RAS patients (n = 20)
Sex	9 males, 10 females	11 males, 9 females
Age	44.1 ± 3.5	44.4 ± 3.5
Smoking history	1 (5.3%)	3 (15%)
Ulcer numbers	-	Single: 13 (65%) Multiple: 7 (35%)
Sampling sites	Lip labial mucosa: 7 (36.8%), Buccal mucosa: 12 (63.2%)	Lip labial mucosa: 4 (20%), Buccal mucosa: 13 (65%) Tongue tip: 3 (15%),
Unstimulated salivary flow rates	0.46 ± 0.08 ml/minute	0.63 ± 0.07 ml/minute

Table 2. Relative abundance of taxa differently distributed between controls and RAU in the mucosal microbiota.

	Controls (n= 19)	RAU (n= 20)	P value
Genus	<i>Veillonella</i> ↓	1.82 (0.49-10.44)	0.82 (0-3.33)
	<i>Acinetobacter</i> ↑	0 (0-2.54)	0.79 (0-7.69)
	<i>Campylobacter</i> ↓	0.22 (0-1.07)	0.08 (0-2.11)
	<i>Lachnoanaerobaculum</i> ↓	0.09 (0.02-0.87)	0.04 (0-0.47)
	<i>Blautia</i> ↑	0 (0-0.24)	0.02 (0-3.73)
	<i>Myxococcus</i> ↑	0 (0-0.14)	0.04 (0-3.73)
	<i>Pseudomonas</i> ↑	0 (0-0.33)	0.02 (0-2.28)
	<i>Atopobium</i> ↓	0.04 (0-0.44)	0 (0-0.42)
	<i>Ruminococcus_g6</i> ↑	0 (0-0.55)	0.02 (0-0.86)
	<i>Moryella</i> ↓	0.04 (0-0.45)	0 (0-0.17)
	<i>Faecalibacterium</i> ↑	0 (0-0.09)	0.01 (0-0.58)
	<i>Staphylococcus</i> ↑	0 (0-0.15)	0.02 (0-0.28)
	<i>Streptococcaceae_uc</i> ↓	0.02 (0-0.06)	0 (0-0.04)
	<i>Flavobacterium</i> ↑	0 (0-0)	0 (0-0.38)
Species	<i>Streptococcus salivarius</i> ↓	4.51 (0.08-18.08)	< 0.0005
	<i>Veillonella dispar</i> ↓	1.54 (0.29-5.30)	0.001
	<i>Streptococcus parasanguinis</i> ↓	1.32 (0-11.45)	0.001
	<i>Acinetobacter oryzae</i> ↑	0 (0-1.1)	0.006
	<i>Actinomyces odontolyticus</i> ↓	0.41 (0-1.73)	0.009
	<i>Veillonella atypica</i> ↓	0.06 (0-4.69)	0.032
	<i>Prevotella melaninogenica</i> ↓	0.12 (0.05-0.85)	0.038
	<i>Acinetobacter johnsonii</i> ↑	0 (0-0.54)	0.001
	<i>FM997095_s</i> ↓	0.2 (0.01-1.35)	0.003
	<i>Streptococcus uc</i> ↓	0.15 (0.03-1.35)	< 0.0005
	<i>Neisseria oralis</i> ↑	0 (0-0.81)	0.025
	<i>HQ757980_s</i> ↓	0.09 (0-1.15)	0.008
	<i>Capnocytophaga granulosa</i> ↓	0.03 (0-2.55)	0.018
	<i>4P002811_s</i> ↓	0.06 (0-1.4)	0.034
	<i>4P003152_s</i> ↓	0.06 (0-1.27)	0.001
	<i>Streptococcus peroris</i> ↓	0.075 (0-0.56)	0.027
	<i>Campylobacter concisus</i> ↓	0.1 (0-0.51)	0.001
	<i>4P003193_s</i> ↓	0.02 (0-2.07)	0.027
	<i>Prevotella histicola</i> ↓	0.01 (0-2.29)	0.007
	<i>Lachnoanaerobaculum orale</i> ↓	0.07 (0.01-0.53)	0.028
	<i>Streptococcus vestibularis</i> ↓	0.02 (0-0.33)	< 0.0005
	<i>Streptococcus lactarius</i> ↓	0.03 (0-0.87)	0 (0-0.1)
	<i>Blautia wexlerae</i> ↑	0 (0-0.24)	0.02 (0-3.21)
	<i>Prevotella saliva</i> e↓	0.01 (0-0.49)	0 (0-0.96)
	<i>DQ447842_s</i> ↓	0.05 (0-0.32)	0.035
	<i>4P002810_s</i> ↓	0.05 (0-0.38)	0.013
	<i>Ruminococcus gnavus</i> ↑	0 (0-0.53)	0.014
	<i>Stomatobaculum longum</i> ↓	0.03 (0-0.45)	0 (0-0.17)
	<i>Bacteroides fragilis</i> ↑	0 (0-0.29)	0.013
	<i>BABG01000051_s</i> ↑	0 (0-0.07)	0.007
	<i>Streptococcaceae uc s</i> ↓	0.02 (0-0.06)	0 < 0.0005

Table 3. Relative abundance of taxa differently distributed between controls and RAU_{AL} in the salivary microbiota.

		Controls (n= 8)	RAU _{AL} (n= 9)	P value
Genus	<i>Streptococcus</i> ↓	25.78 (12.10-44.24)	13.05 (3.5-26.86)	0.034
	<i>Porphyromonas</i> ↑	0.51 (0.17-2.65)	3.43 (0.23-12.27)	0.016
	<i>Capnocytophaga</i> ↑	0.93 (0.19-6.43)	2.56 (1.55-10.43)	0.043
	<i>GU410548_g</i> ↑	0.02 (0-0.03)	0.07 (0-4.72)	0.014
	<i>Abiotrophia</i> ↑	0 (0-0.09)	0.04 (0-0.28)	0.017
	<i>Escherichia</i> ↓	0.05 (0-0.17)	0 (0-0.03)	0.033
Species	<i>AM420091_s</i> ↑	0.24 (0-1.94)	1.53 (0.17-10.64)	0.043
	<i>Streptococcus salivarius</i> ↓	3.22 (0.76-10.42)	0.71 (0.03-3.84)	0.007
	<i>Streptococcus parasanguinis</i> ↓	0.98 (0.24-8.42)	0.33 (0.03- 1.11)	0.043
	<i>Capnocytophaga gingivalis</i> ↑	0.19 (0.04- 0.62)	0.73 (0.04- 3.5)	0.009
	<i>Neisseria flava</i> ↑	0 (0-0.1)	0.32 (0-6.99)	0.003
	<i>Rothia dentocariosa</i> ↓	0.97 (0.06-2.31)	0.28 (0-0.69)	0.043
	<i>HQ767899_s</i> ↓	0.44 (0.02-2.97)	0.04 (0-1.29)	0.034
	<i>Aggregatibacter segnis</i> ↑	0.03 (0-0.19)	0.28 (0-2.65)	0.023
	<i>Capnocytophaga sputigena</i> ↑	0.05 (0-0.2)	0.36 (0.06-1.62)	0.003
	<i>4P003196_s</i> ↑	0.04 (0.01-0.42)	0.14 (0.1- 2.09)	0.021
	<i>Neisseria sicca group</i> ↓	0.25 (0-6.62)	0 (0-0)	< 0.0005
	<i>Actinomyces viscosus</i> ↓	0.05 (0-1.37)	0 (0-0.16)	0.028
	<i>HQ757980_s</i> ↓	0.1 (0.03-0.88)	0 (0-0.74)	0.032
	<i>4P004176_s</i> ↑	0 (0-0.03)	0.04 (0-0.23)	0.015
	<i>Porphyromonas catoniae</i> ↑	0 (0-0.01)	0.03 (0-0.23)	0.029
	<i>Escherichia coli</i> group ↓	0.06 (0-0.17)	0 (0-0.03)	0.033
	<i>AM420214_s</i> ↑	0 (0-0.01)	0.01 (0- 0.13)	0.021