The early diagnosis and monitoring of squamous cell carcinoma via saliva metabolomics

Qihui Wang[1], Pan Gao[2], Xiaoyi Wang[2], Yixiang Duan*[,1]

[1]*Research Center of Analytical Instrumentation, College of Life Science, Sichuan University, Chengdu 610064, P. R. China*

[2]*Department of Head and Neck Oncology, West China College of Stomatology, Sichuan University, Chengdu 610064, P. R. China*

Supplemental Table 1. Clinical characteristics of saliva samples used in this study

Characteristics	OSCC patients	Healthy controls
Number of subjects	30	30
Race	Chinese	Chinese
Gender (Male/Female)	25/5	25/5
Age (mean, range)	55, 29-72	47, 25-69
Clinical staging		
Early stage (I-II)	13 (I:4, II:9)	
Advanced stage (III-IV)	17 (III:3, IV:14)	
TNM staging [a]		
Tumor states (T)	T1:7, T2:10, T3:1, T4:12	
Regional lymph node status (N)	N0:18, N1:9, N2:3	
Distant metastasis status (M)	M0:30, M1:0	

[a]cTNM.

Supplemental Figure 1. Metabonomics research strategy with the integration of RPLC and HILIC for OSCC salivary biomarkers identification.
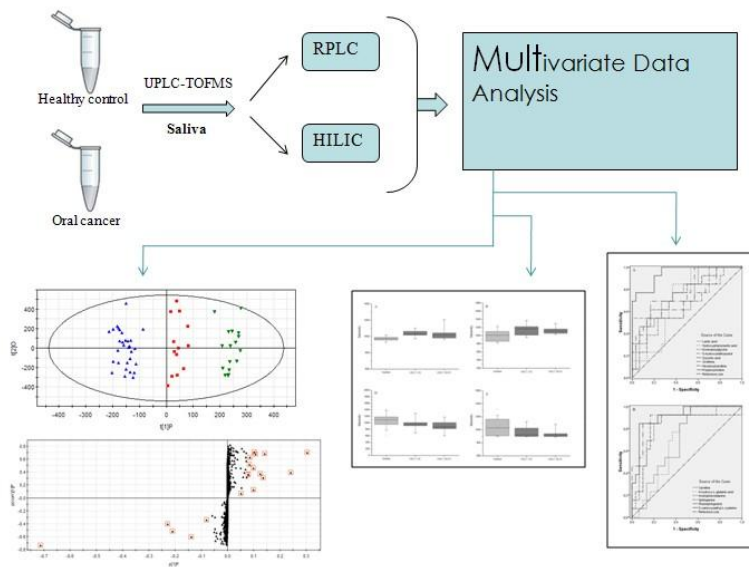
Supplemental Figure 2. The elemental composition analysis for the ion of *m/z* 89.0226/2.59 min in HILIC with negative-ion mode.
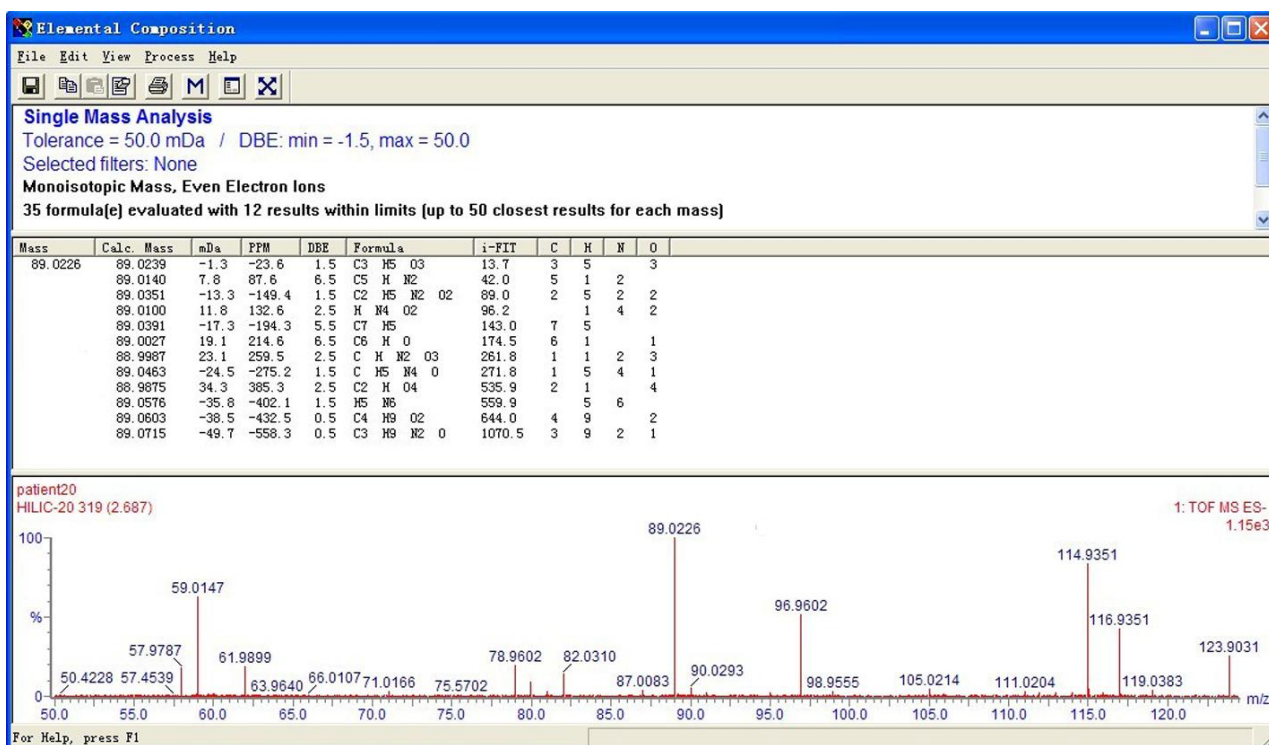
Supplemental Figure 3. Phenylalanine metabolism

PHENYLALANINE METABOLISM

Norpseudoephedrine
Pseudoephedrine
1-Phenylpropane-1,2-dione
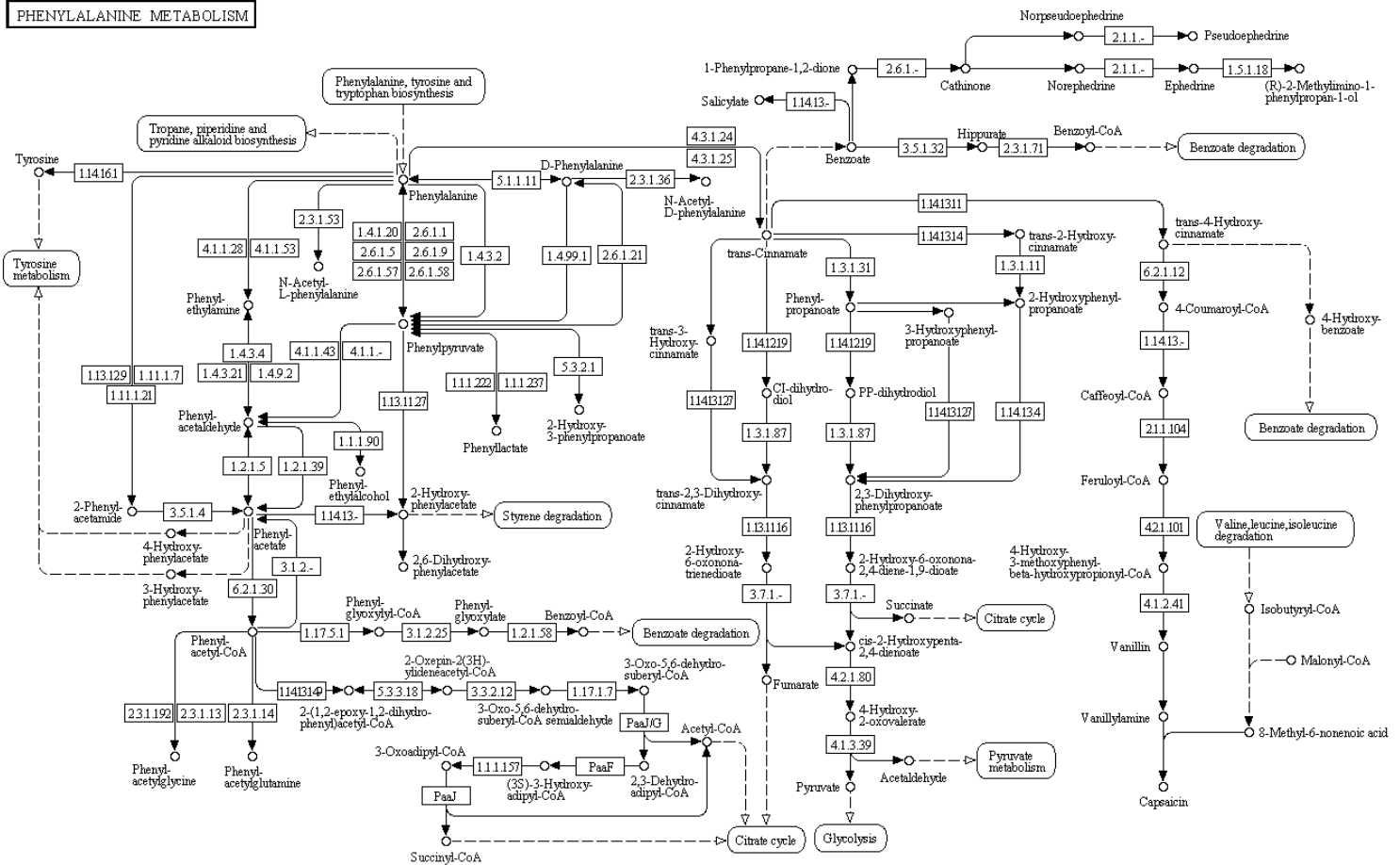2.6.1.-
Cathinone
2.1.1.-
2.1.1.-
Norephedrine
Ephedrine
1.5.1.18
(R)-2-Methylimino-1-phenylpropan-1-ol
Salicylate
1.14.13.-
Benzoate
3.5.1.32
Hippurate
2.3.1.71
Benzoyl-CoA
Benzoate degradation

Phenylalanine, tyrosine and tryptophan biosynthesis

4.3.1.24
4.3.1.25
D-Phenylalanine
5.1.1.11
2.3.1.36
N-Acetyl-D-phenylalanine

Tropane, piperidine and pyridine alkaloid biosynthesis

Tyrosine
1.14.16.1
Phenylalanine

Tyrosine metabolism

1.14.13.11
trans-2-Hydroxy-cinnamate
trans-4-Hydroxy-cinnamate
1.14.13.14
6.2.1.12
4-Coumaroyl-CoA
1.14.13.-
4-Hydroxy-benzoate

2.3.1.53
4.1.1.28
4.1.1.53
1.4.1.20
2.6.1.1
2.6.1.5
2.6.1.9
2.6.1.57
2.6.1.58
1.4.3.2
1.4.99.1
2.6.1.21
N-Acetyl-L-phenylalanine

Phenyl-ethylamine

trans-Cinnamate
1.3.1.31
Phenyl-propanoate
2-Hydroxyphenyl-propanoate
1.14.13.-
Caffeoyl-CoA

1.3.1.11
Phenylpyruvate

1.13.129
1.11.1.7
1.11.1.21
1.4.3.4
1.4.3.21
4.1.1.43
1.4.9.2
4.1.1.-
1.1.1.222
1.1.1.237
5.3.2.1
1.13.11.27
2-Hydroxy-3-phenylpropanoate

trans-3-Hydroxy-cinnamate
1.14.13.127
1.14.12.19
Cl-dihydro-diol
1.14.12.19
PP-dihydrodiol
3-Hydroxyphenyl-propanoate
1.14.13.127
1.14.13.4
2.1.1.104

Phenyl-acetaldehyde
Phenyllactate
1.1.1.90
1.3.1.87
1.3.1.87
Feruloyl-CoA

1.2.1.5
1.2.1.39
Phenyl-ethylalcohol
2-Hydroxy-phenylacetate
Styrene degradation
trans-2,3-Dihydroxy-cinnamate
1.13.11.16
2,3-Dihydroxy-phenylpropanoate
1.13.11.16
4.2.1.101
Valine, leucine, isoleucine degradation

2-Phenyl-acetamide
3.5.1.4
Phenyl-acetate
1.14.13.-
2,6-Dihydroxy-phenylacetate
2-Hydroxy-6-oxonona-trienedioate
3.7.1.-
2-Hydroxy-6-oxonona-2,4-diene-1,9-dioate
3.7.1.-
4-Hydroxy-3-methoxyphenyl-beta-hydroxypropionyl-CoA
4.1.2.41
Vanillin

4-Hydroxy-phenylacetate
3.1.2.-
Succinate
Citrate cycle
Isobutyryl-CoA

3-Hydroxy-phenylacetate
6.2.1.30
Phenyl-acetyl-CoA
Phenyl-glyoxylyl-CoA
1.17.5.1
Phenyl-glyoxylate
1.2.1.58
Benzoyl-CoA
Benzoate degradation
cis-2-Hydroxypenta-2,4-dienoate
4.2.1.80
4-Hydroxy-2-oxovalerate
Vanillylamine
Malonyl-CoA

2.3.1.192
2.3.1.13
2.3.1.14
1.14.13.149
2-Oxepin-2(3H)-ylideneacetyl-CoA
5.3.3.18
3.3.2.12
3-Oxo-5,6-dehydro-suberyl-CoA
1.17.1.7
3-Oxo-5,6-dehydro-suberyl-CoA
PaaJ/G
Acetyl-CoA
4.1.3.39
Pyruvate
Acetaldehyde
Pyruvate metabolism
8-Methyl-6-nonenoic acid

2-(1,2-epoxy-1,2-dihydro-phenyl)acetyl-CoA
3-Oxo-5,6-dehydro-suberyl-CoA semialdehyde

Phenyl-acetylglycine
Phenyl-acetylglutamine
3-Oxoadipyl-CoA
1.1.1.157
PaaF
2,3-Dehydro-adipyl-CoA
PaaJ
(3S)-3-Hydroxy-adipyl-CoA
Fumarate
Capsaicin

Succinyl-CoA
Citrate cycle
Glycolysis

00360 6/17/13
(c) Kanehisa Laboratories

Supplemental Figure 4. Sphingolipid metabolism