Supporting information:

Development of a multiplexed LC-MRM/MS method for evaluation of salivary proteins as oral cancer biomarkers

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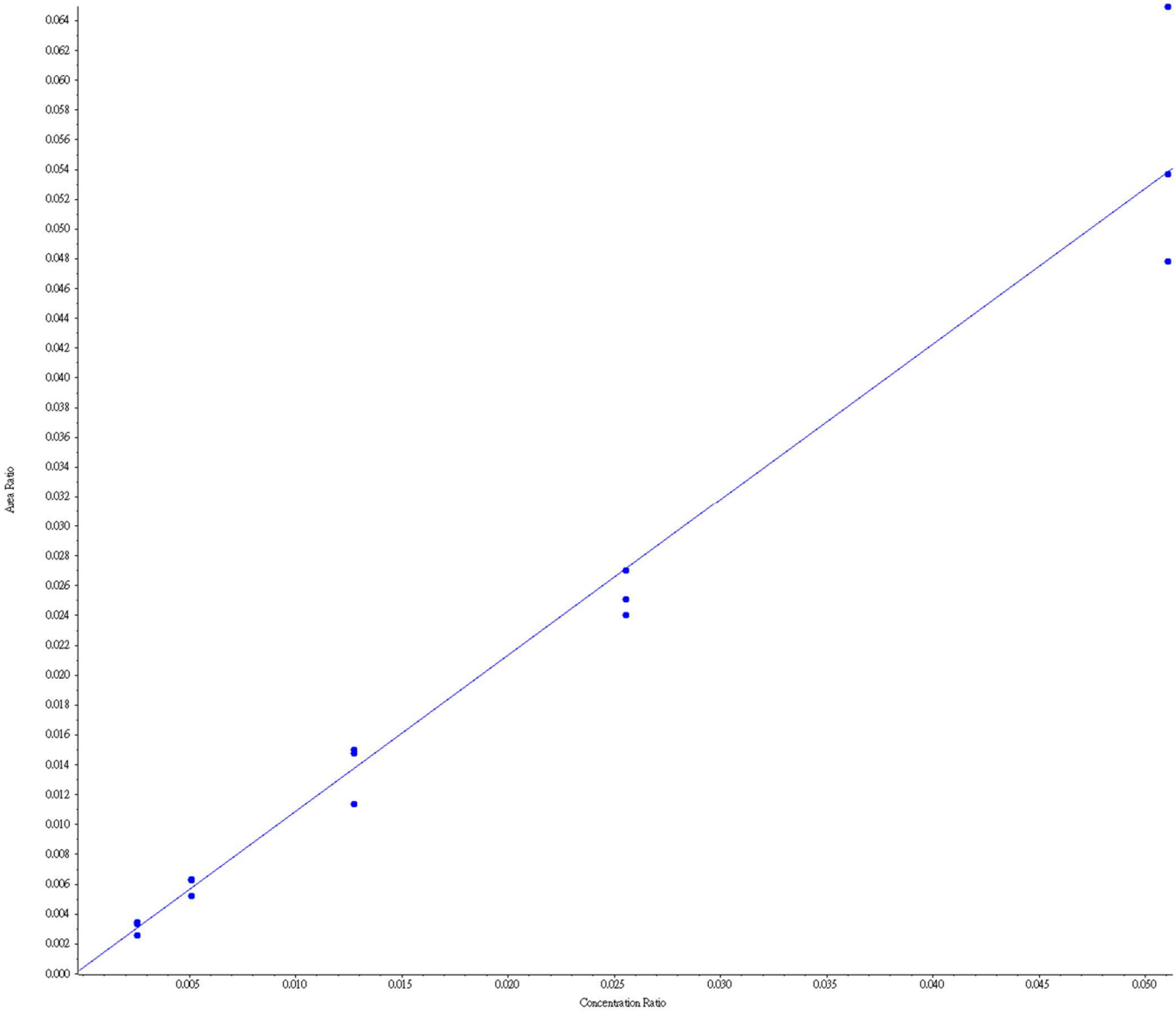
Supplemental Figure S1A. Calibration Curves

The following shows the calibration curve for each analyte. Note that for this example data this is the externally imported calibration.

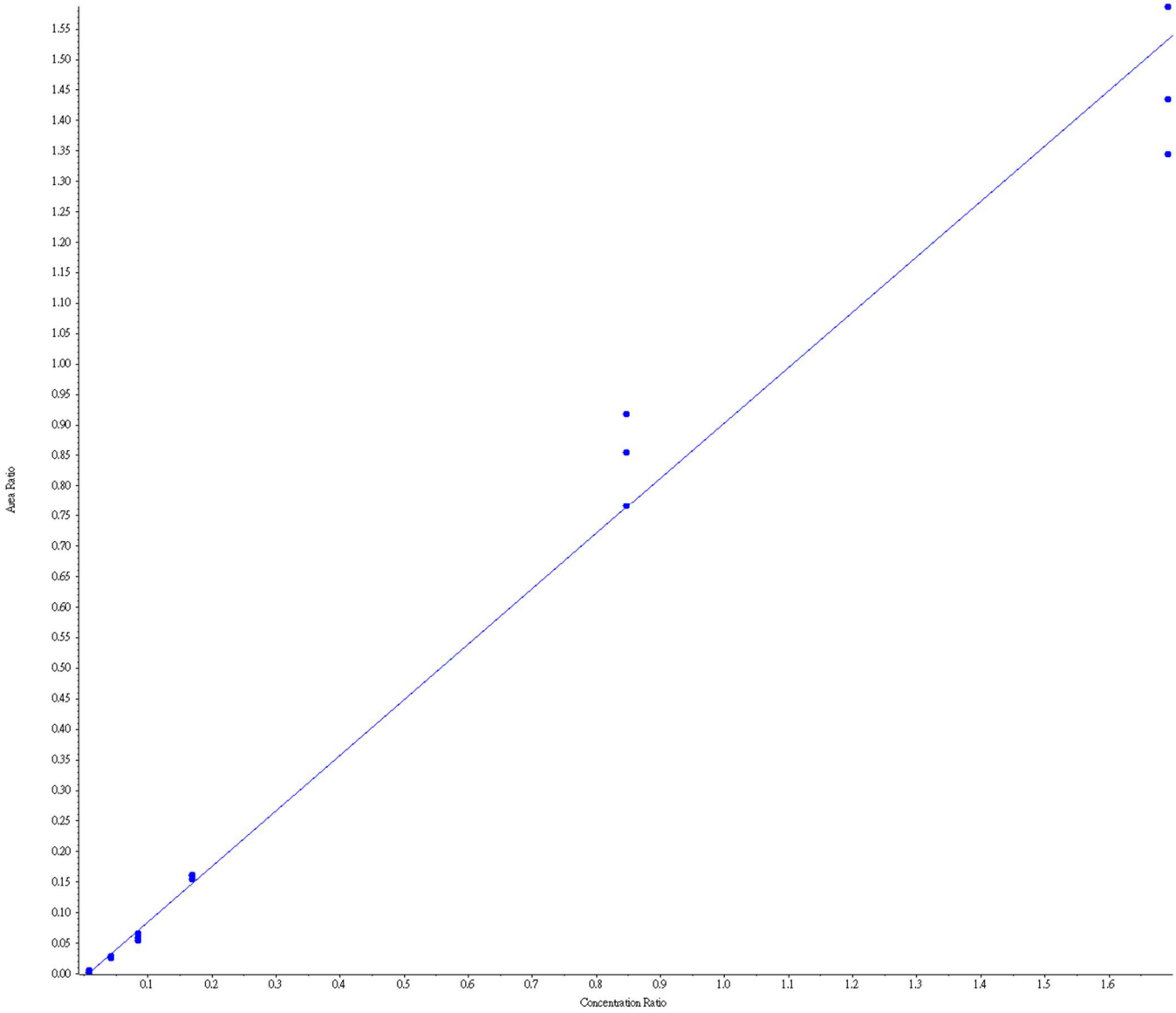
Analyte Name: **ADIPO.IFYNQQNHYDGSTGK.3/y13(2+).M00**

Calibration Equation: y = 1.04622 x + 4.22291e-4 (r = 0.98883) (weighting: 1 / x)



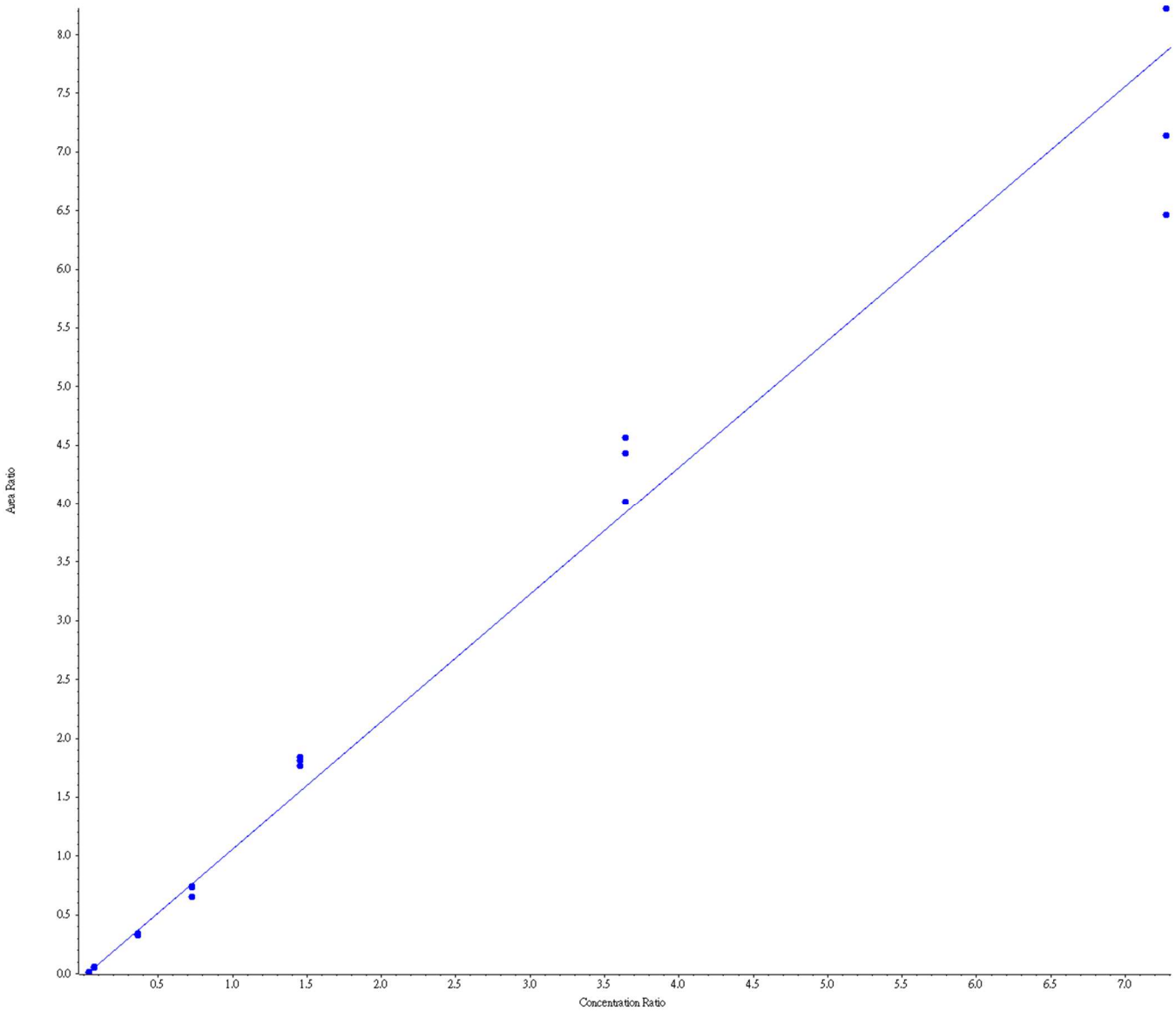
Analyte Name: **AFAM.DADPDTFFAK.2/y7(2+).M00**

Calibration Equation: y = 0.90958 x + -0.00603 (r = 0.99404) (weighting: 1 / x)



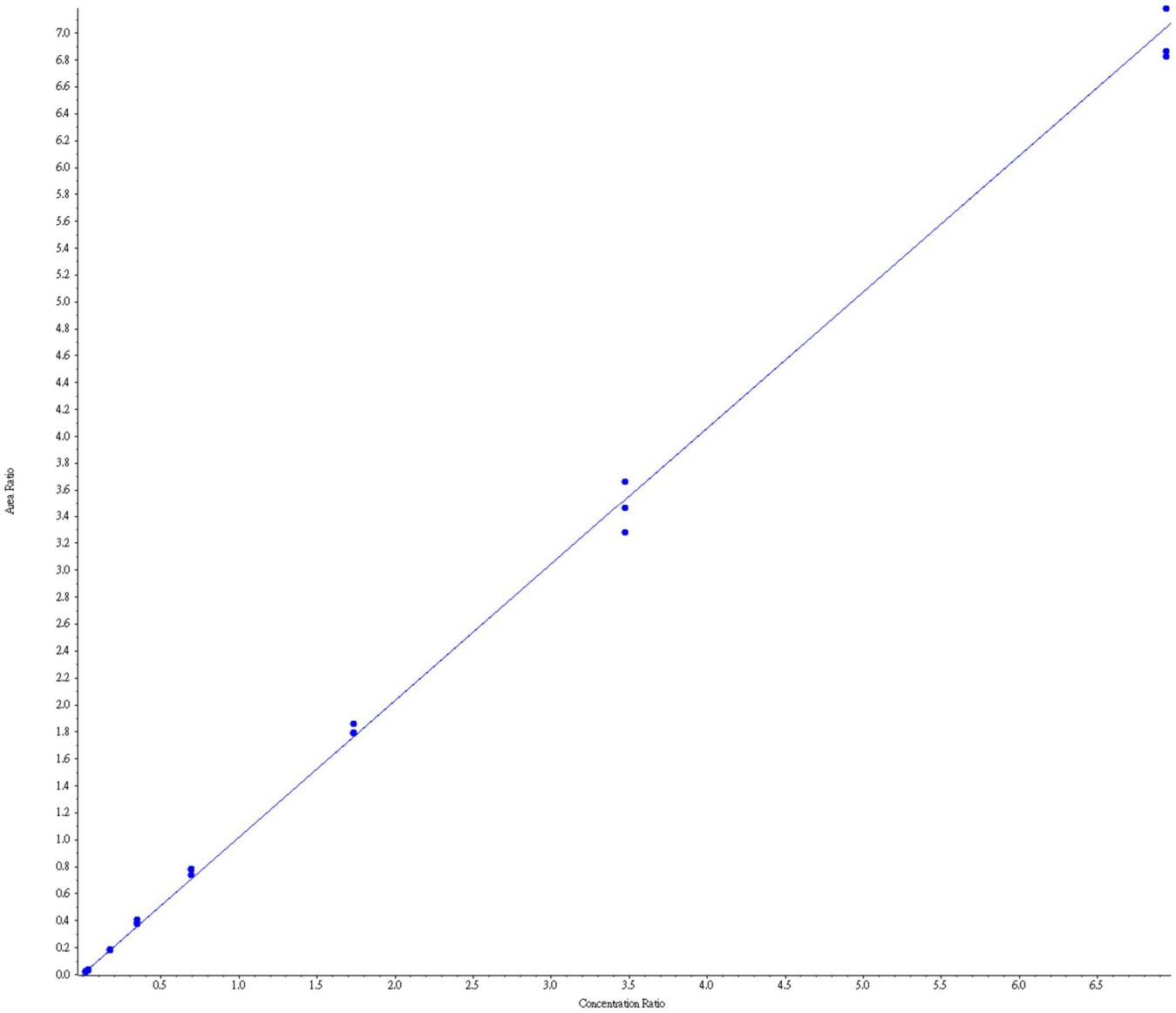
Analyte Name: **A1AT.LSITGTYDLK.2/y6.M00**

Calibration Equation: y = 1.08350 x + -0.02503 (r = 0.99203) (weighting: 1 / x)



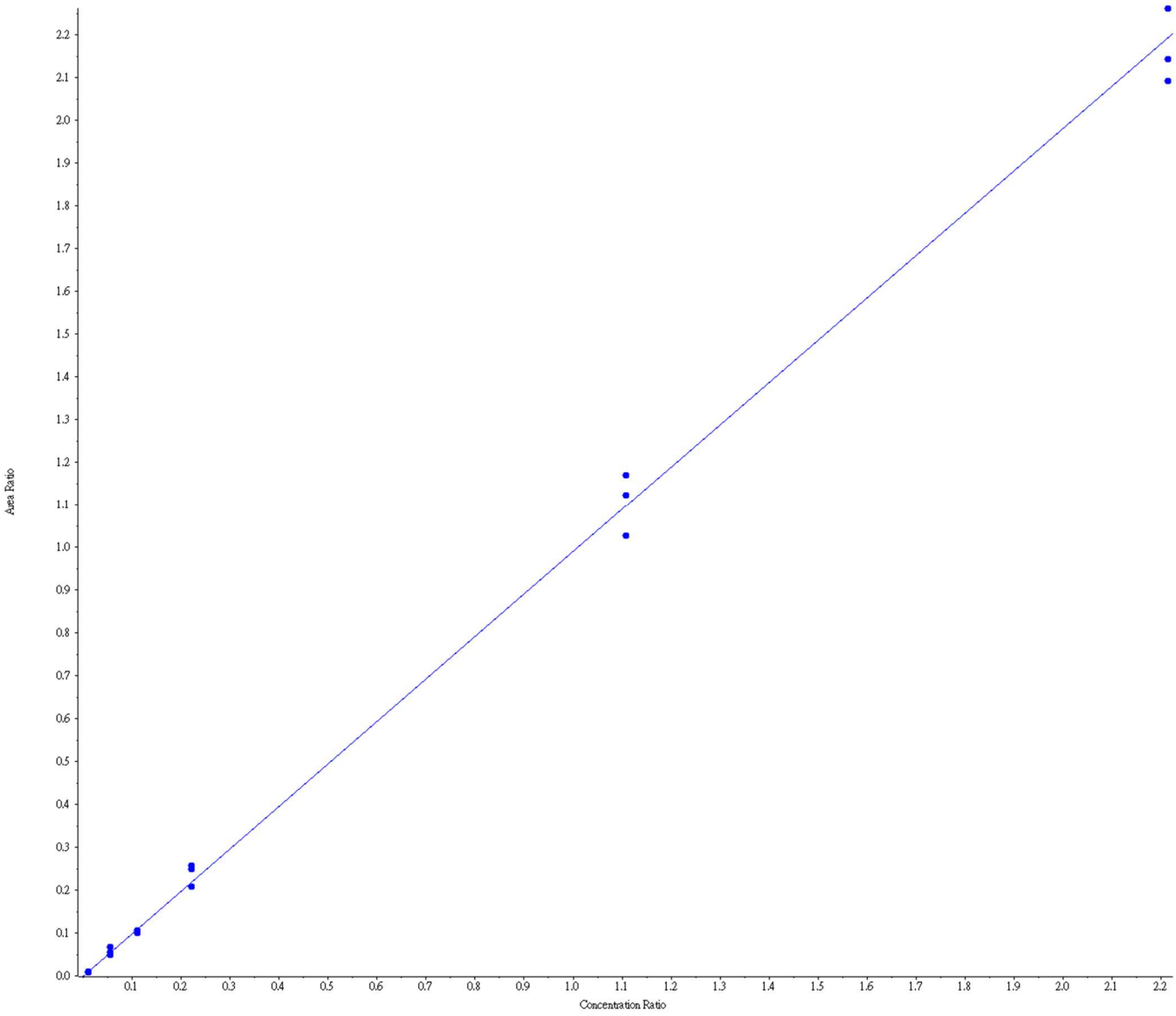
Analyte Name: **FETUA.HTLNQIDEVK.3/y4.M00**

Calibration Equation: y = 1.01389 x + 0.00588 (r = 0.99906) (weighting: 1 / x)



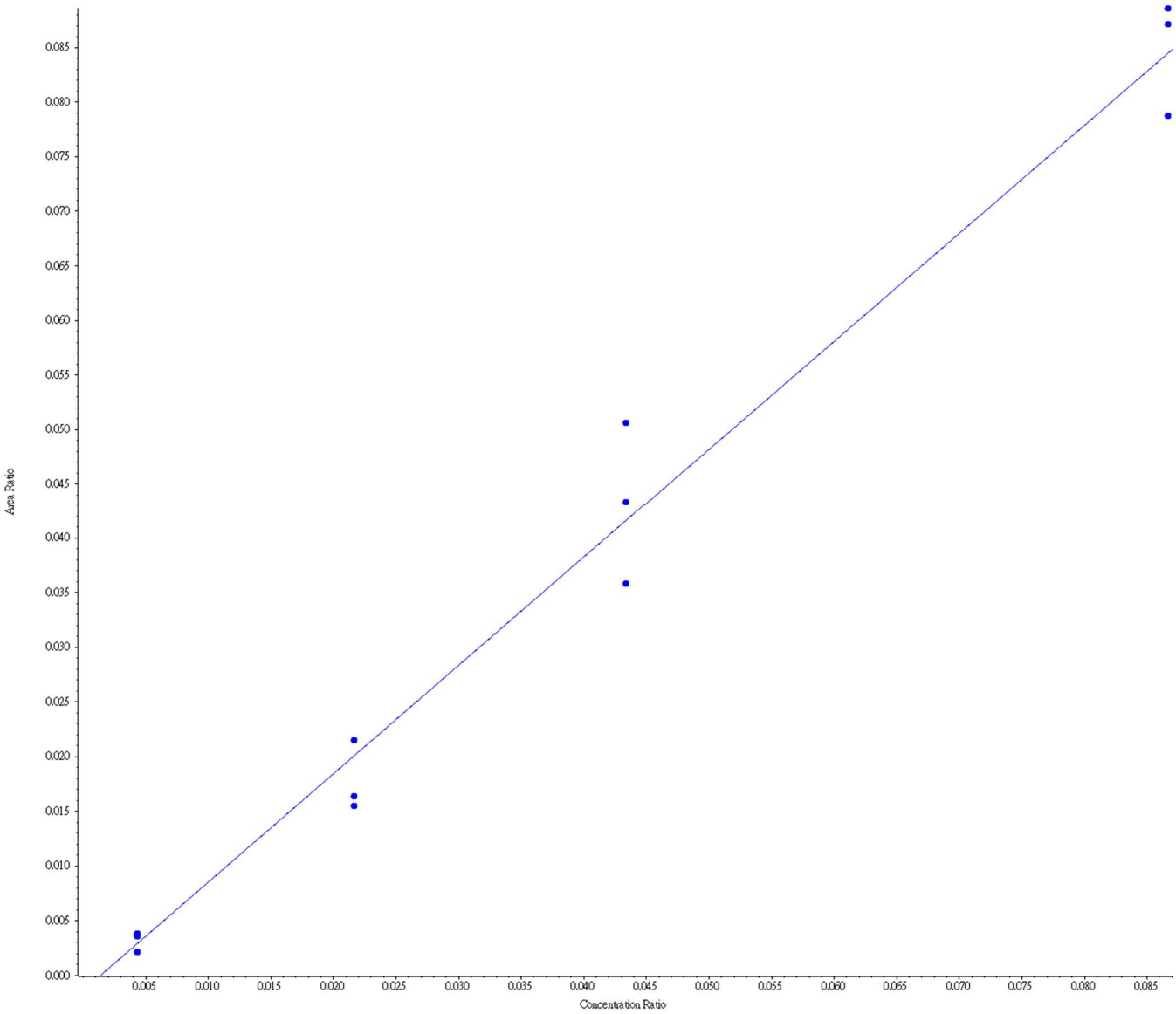
Analyte Name: **ANGT.ALQDQLVLVAAK.2/y10(2+).M00**

Calibration Equation: y = 0.99112 x + -0.00102 (r = 0.99832) (weighting: 1 / x)



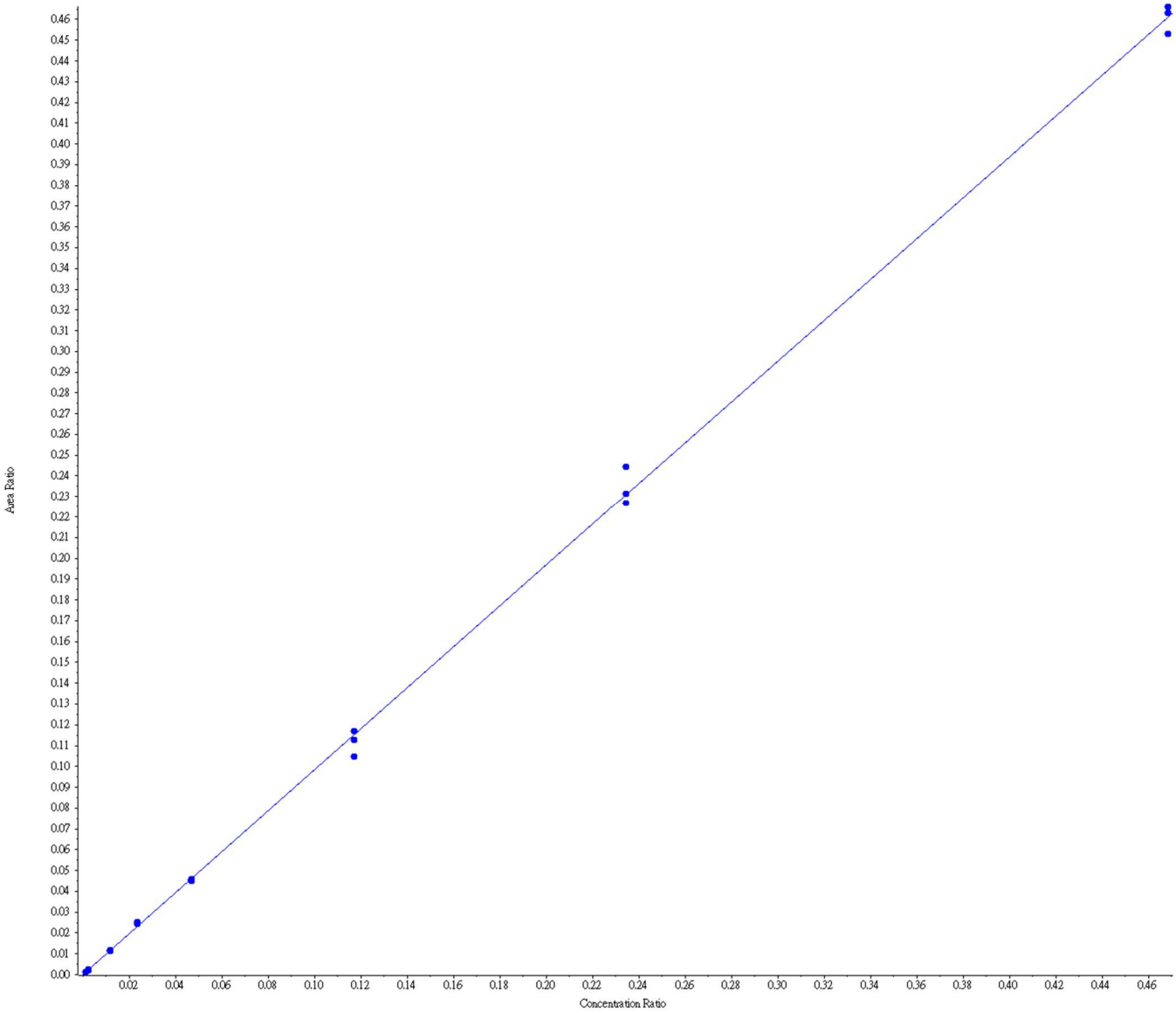
Analyte Name: **ANXA5.GTVTDFPGFDER.2/y6.M00**

Calibration Equation: y = 0.99055 x + -0.00136 (r = 0.99120) (weighting: 1 / x)



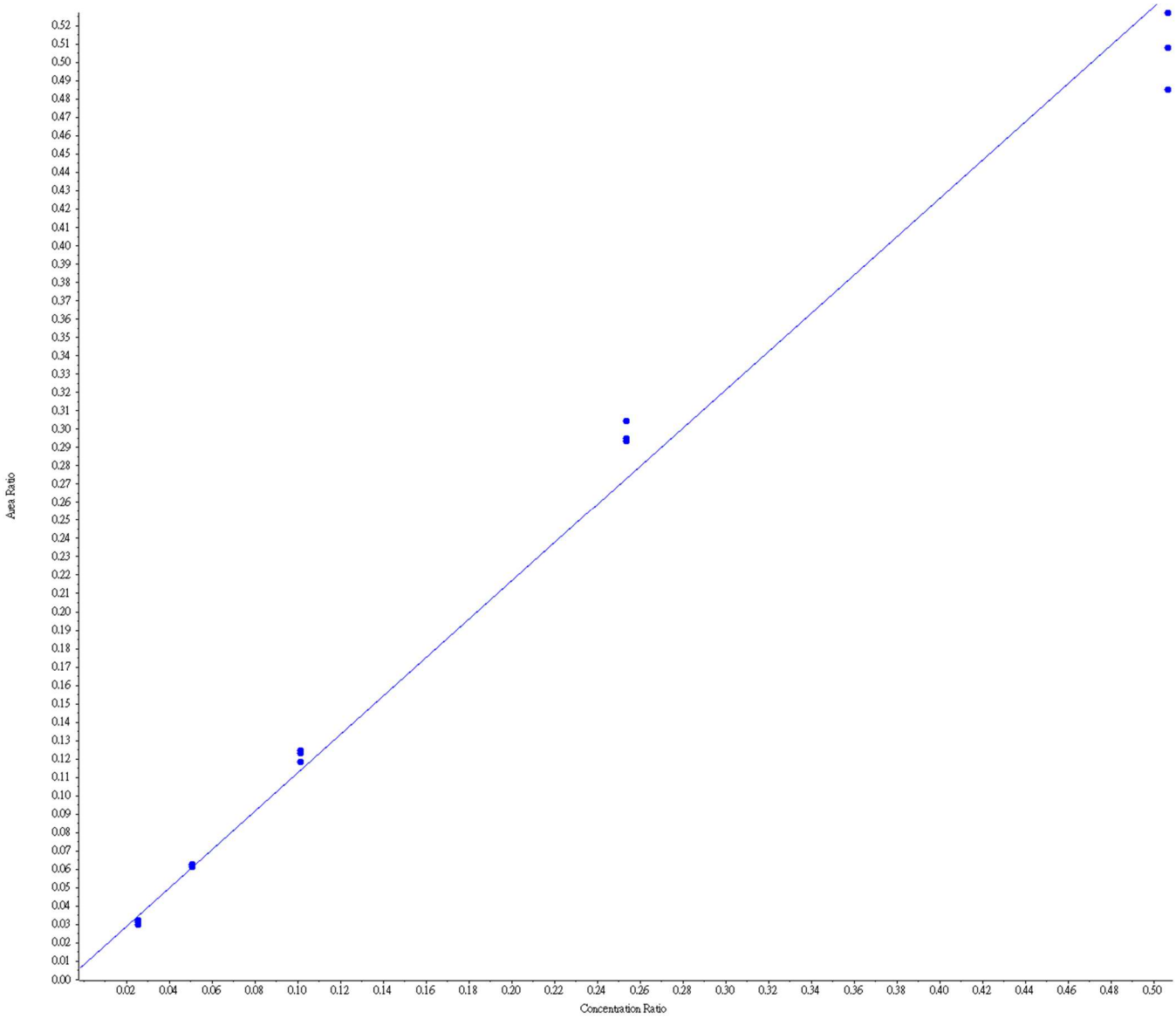
Analyte Name: **APOA1.ATEHLSTLSEK.3/y9(2+).M00**

Calibration Equation: y = 0.98413 x + 1.17532e-4 (r = 0.99948) (weighting: 1 / x)



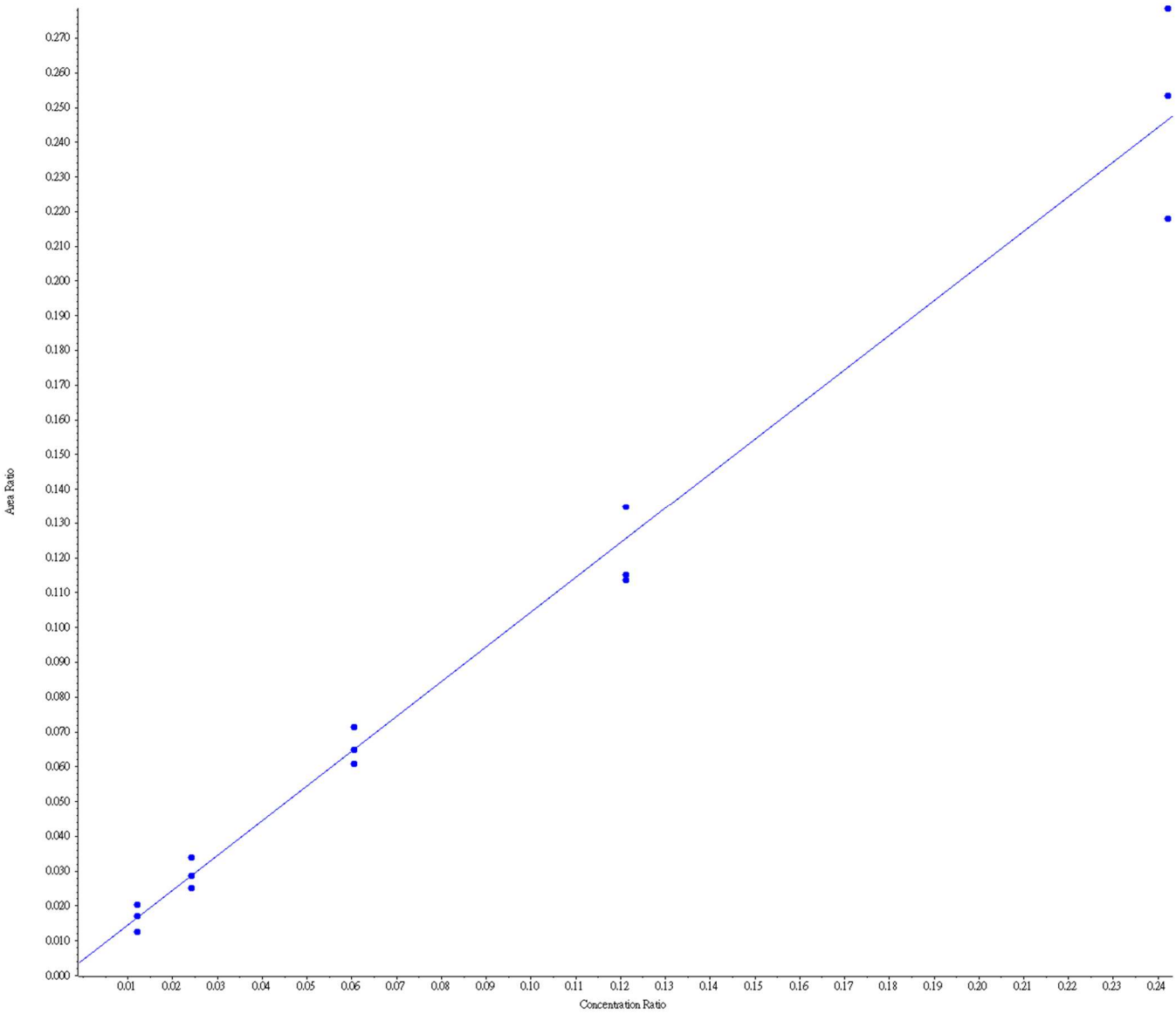
Analyte Name: **APOA2.SPELQAEAK.2/y8(2+).M00**

Calibration Equation: y = 1.04409 x + 0.00822 (r = 0.99529) (weighting: 1 / x)



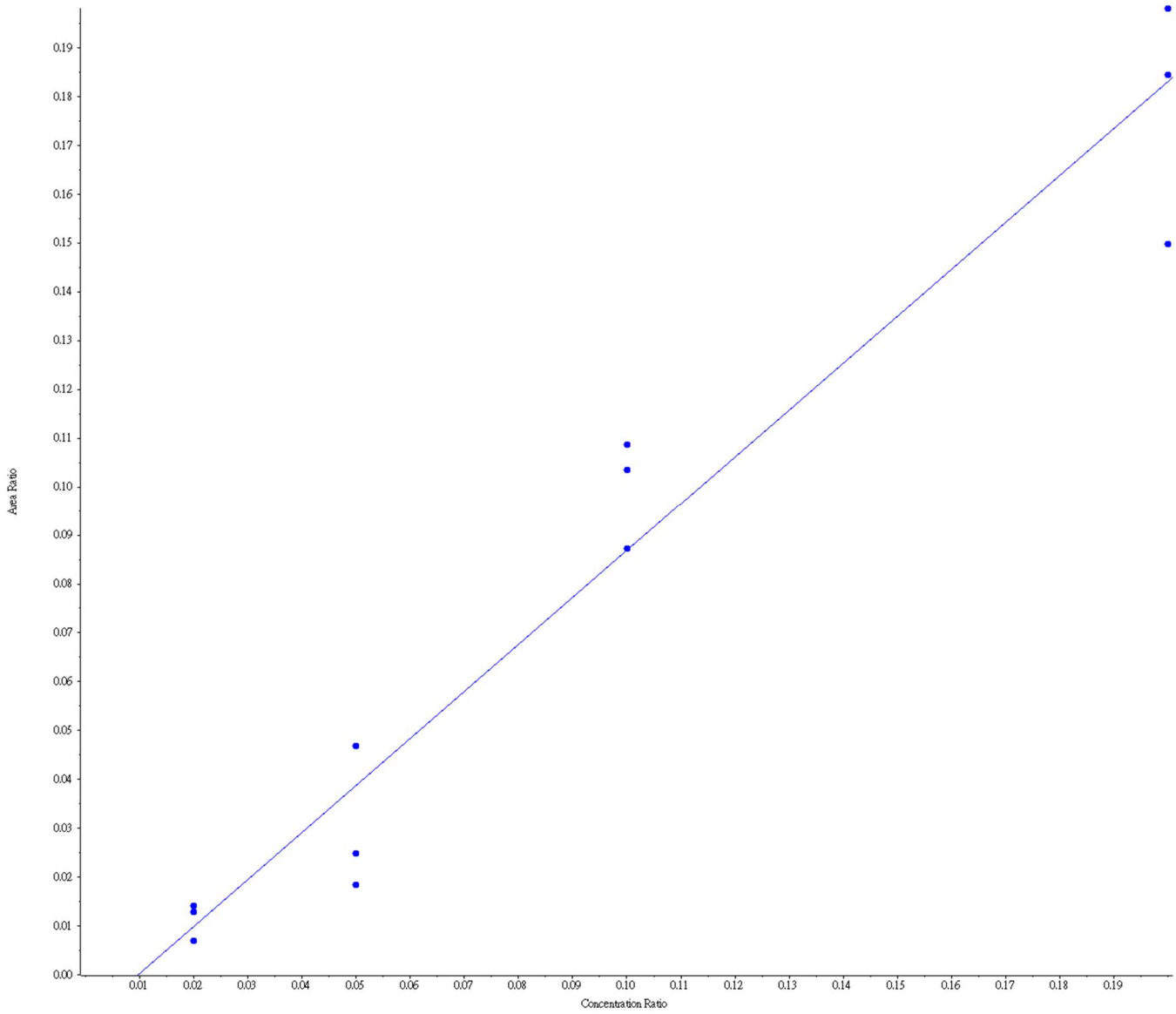
Analyte Name: **APOA4.SLAPYAQDTQEK.2/y9(2+).M00**

Calibration Equation: y = 0.99889 x + 0.00457 (r = 0.99132) (weighting: 1 / x)



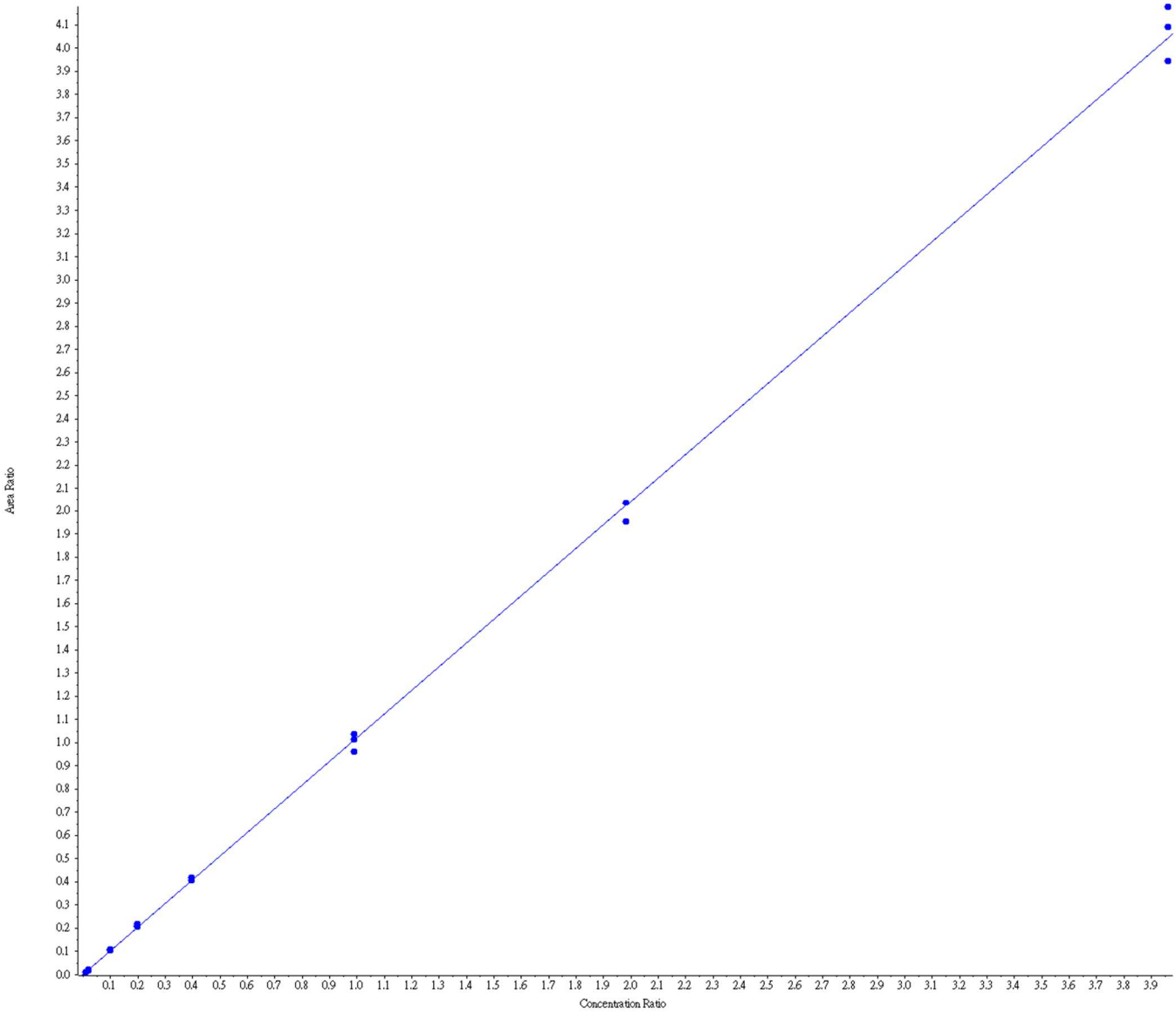
Analyte Name: **APOL1.VTEPISAESGEQVER.2/y12(2+).M00**

Calibration Equation: y = 0.96241 x + -0.00935 (r = 0.97204) (weighting: 1 / x)



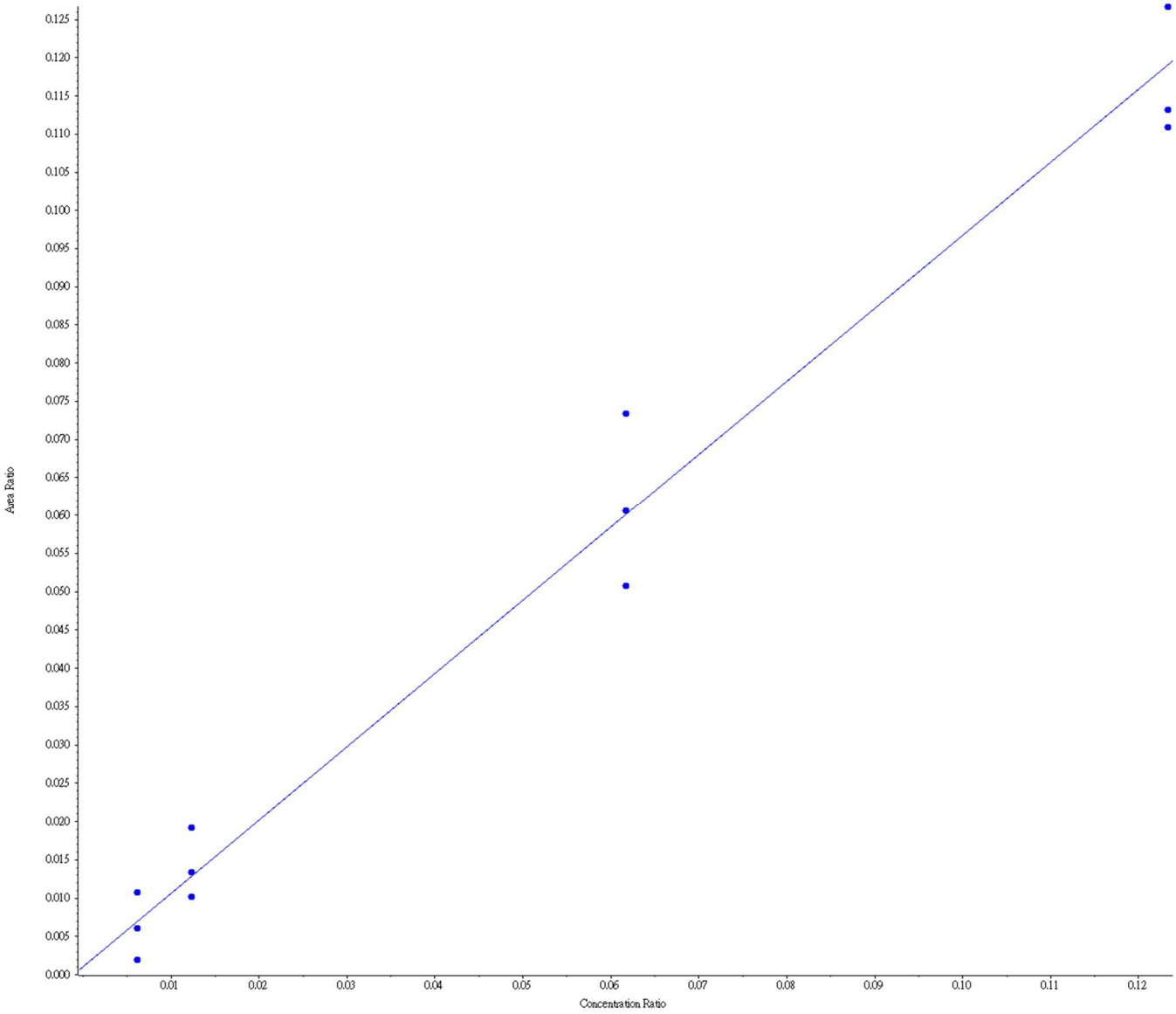
Analyte Name: **APOH.ATVVYQGER.2/y6.M00**

Calibration Equation: y = 1.02064 x + 0.00157 (r = 0.99957) (weighting: 1 / x)



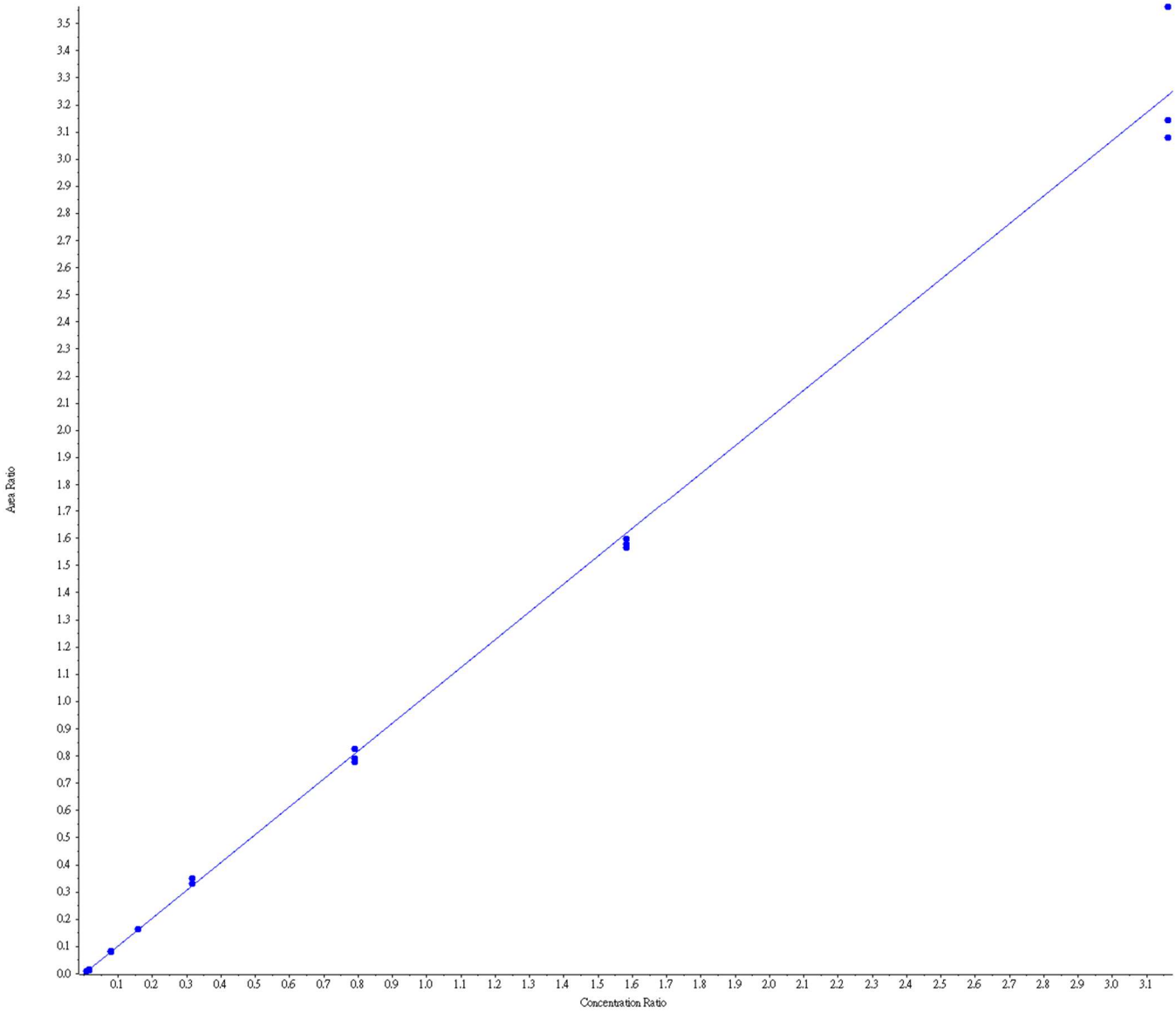
Analyte Name: **CO9.TEHYEEQIEAFK.3/b5.M00**

Calibration Equation: y = 0.95696 x + 0.00105 (r = 0.98030) (weighting: 1 / x)



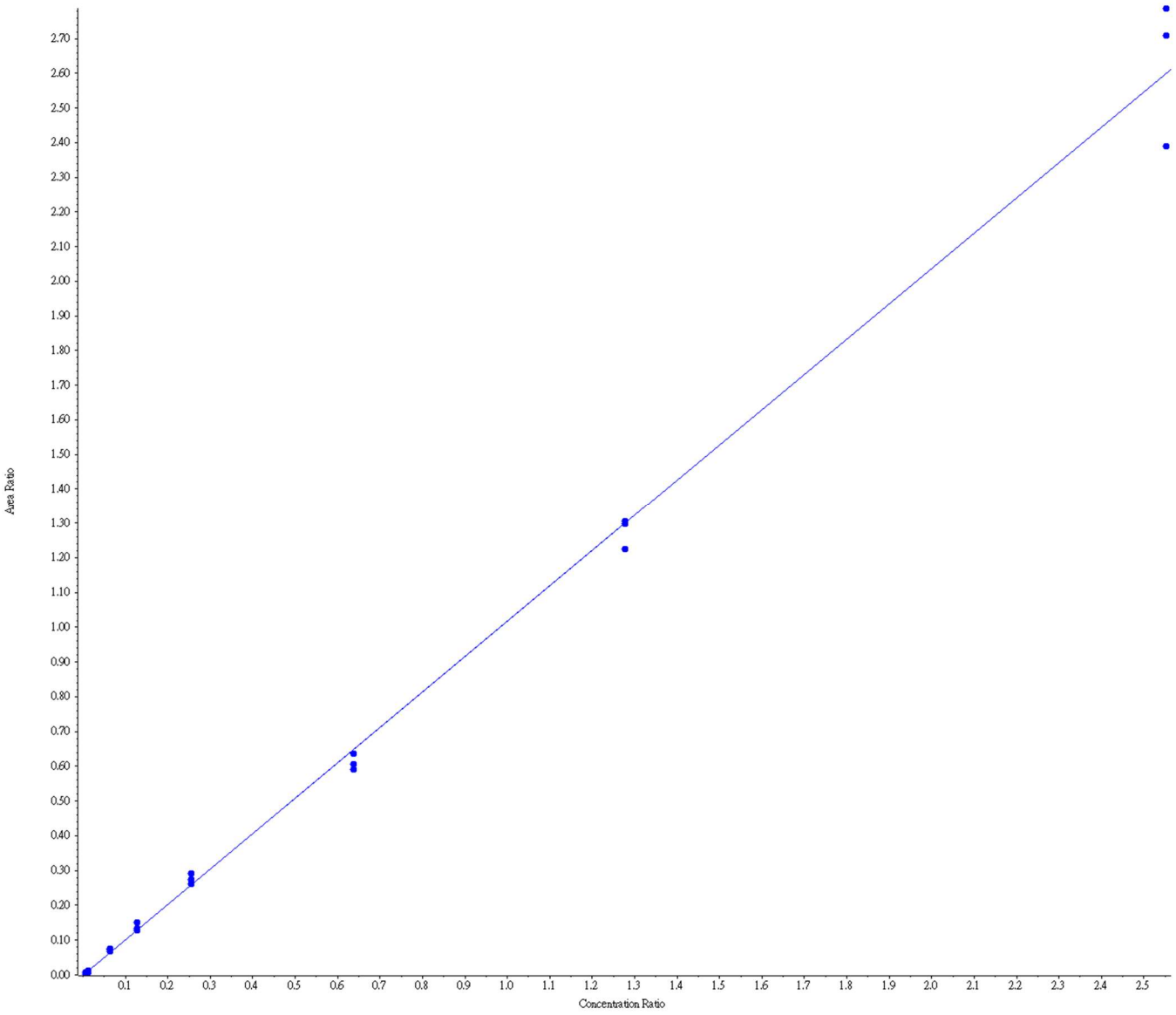
Analyte Name: **FIBB.QGFGNVATNTDGK.2/y7.M00**

Calibration Equation: y = 1.02320 x + 7.59790e-5 (r = 0.99848) (weighting: 1 / x)



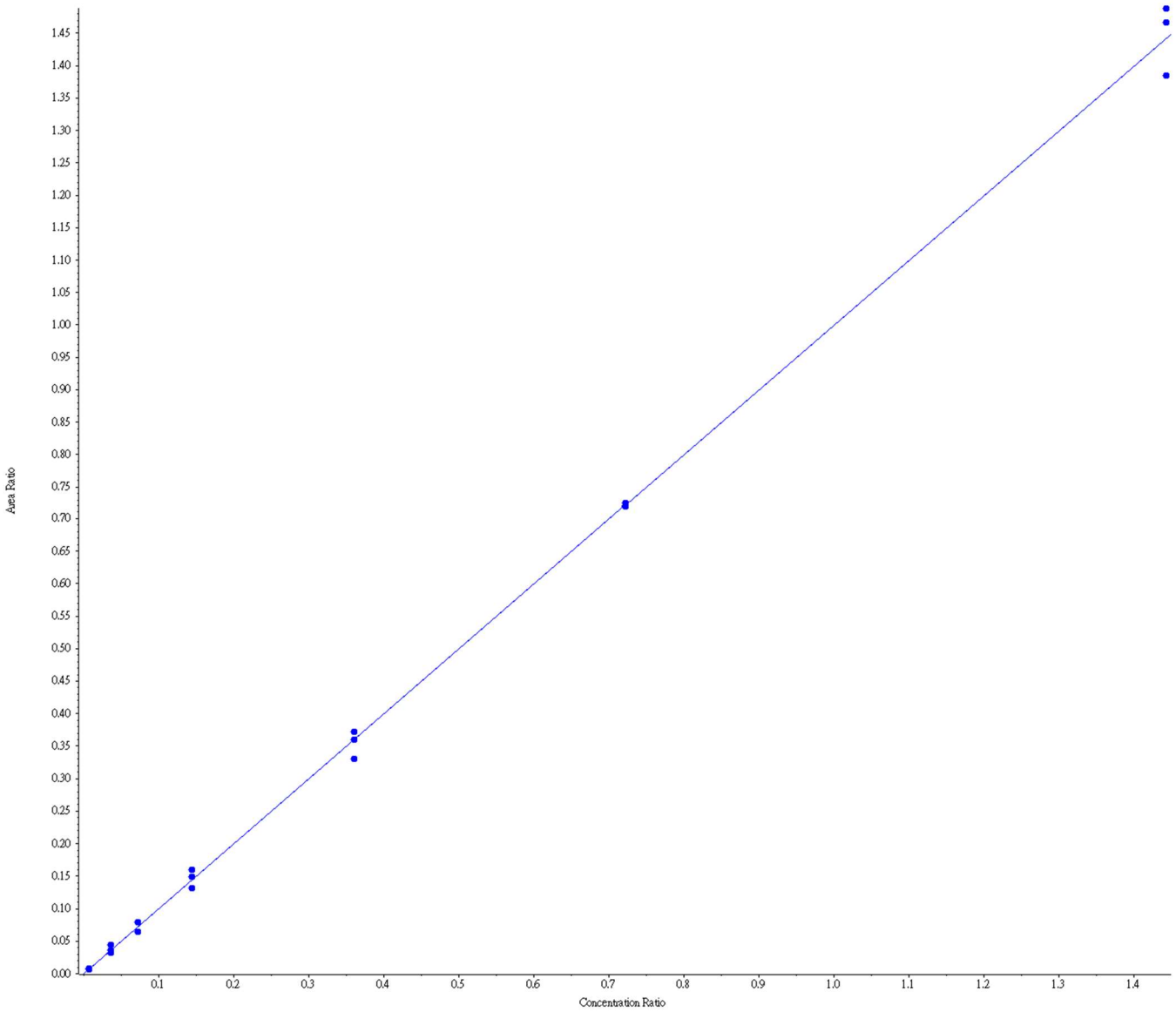
Analyte Name: **ITIH1.AAISGENAGLVR.2/y9.M00**

Calibration Equation: y = 1.01891 x + -0.00102 (r = 0.99781) (weighting: 1 / x)



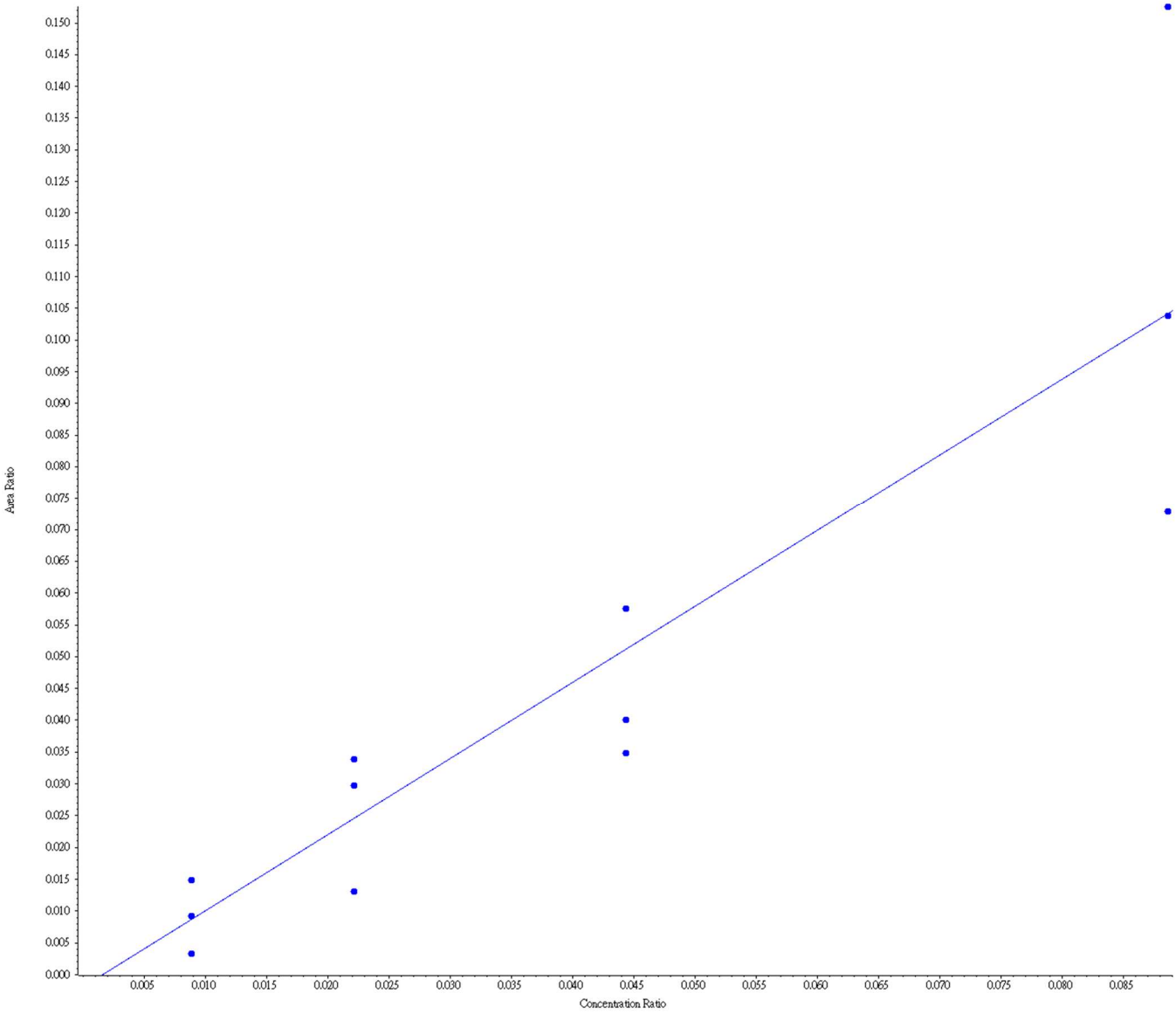
Analyte Name: **PLMN.LFLEPTR.2/y5.M00**

Calibration Equation: y = 0.99955 x + 4.11239e-5 (r = 0.99900) (weighting: 1 / x)



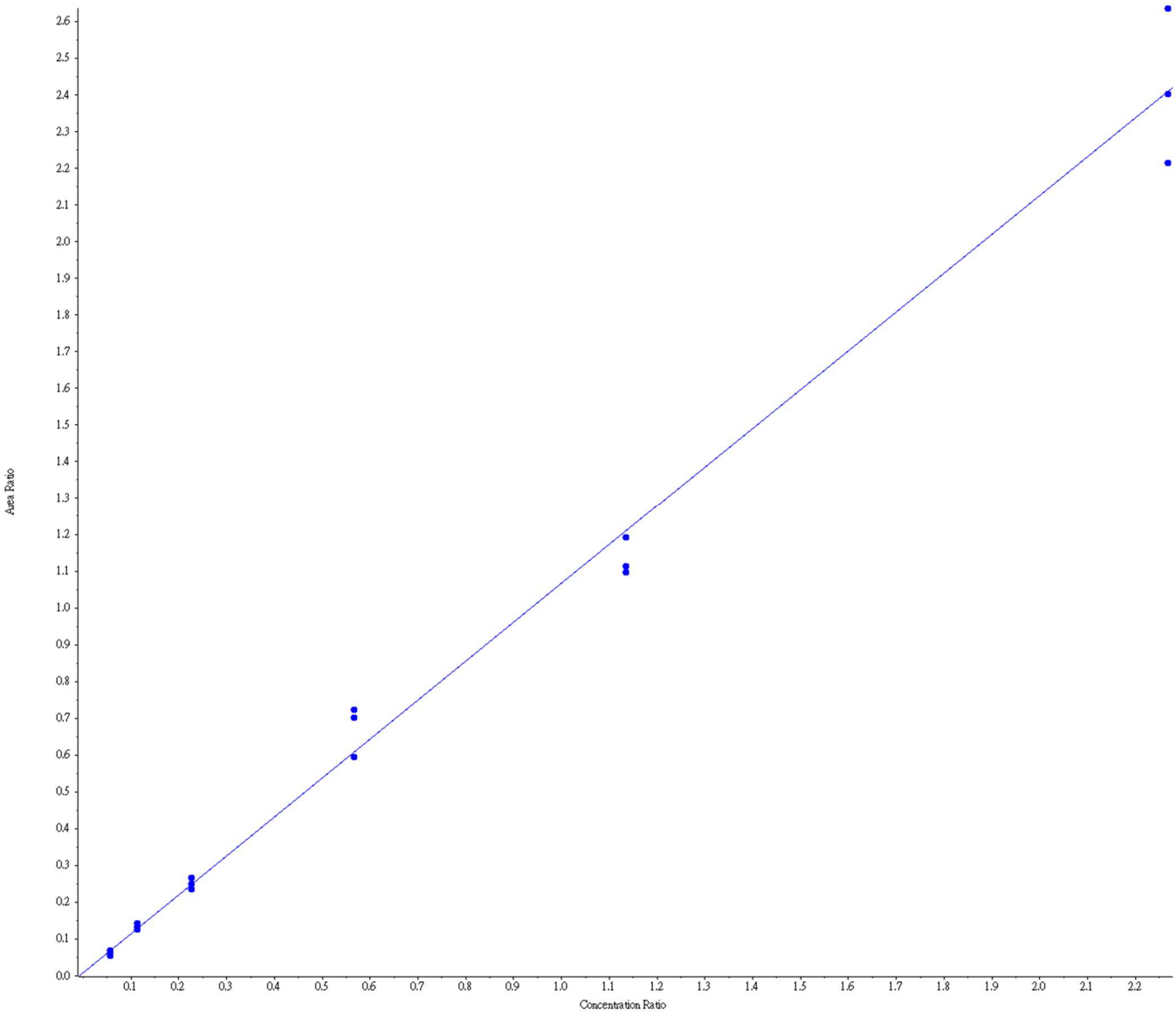
Analyte Name: **THRB.ETAASLLQAGYK.2/y8.M00**

Calibration Equation: y = 1.19617 x + -0.00189 (r = 0.91662) (weighting: 1 / x)



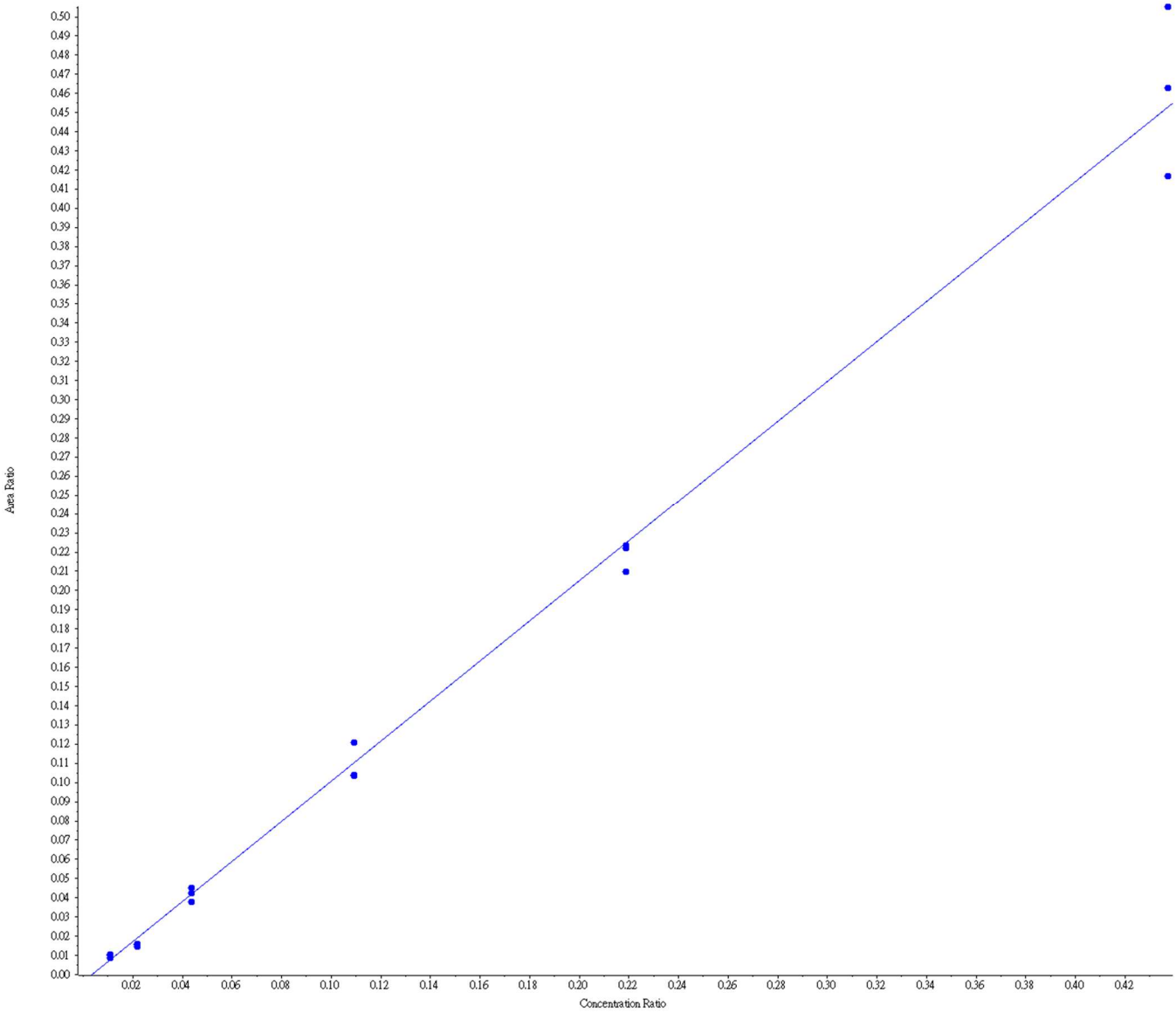
Analyte Name: **SAA4.GPGGVWAAK.2/y8(2+).M00**

Calibration Equation: y = 1.05874 x + 0.00846 (r = 0.99524) (weighting: 1 / x)



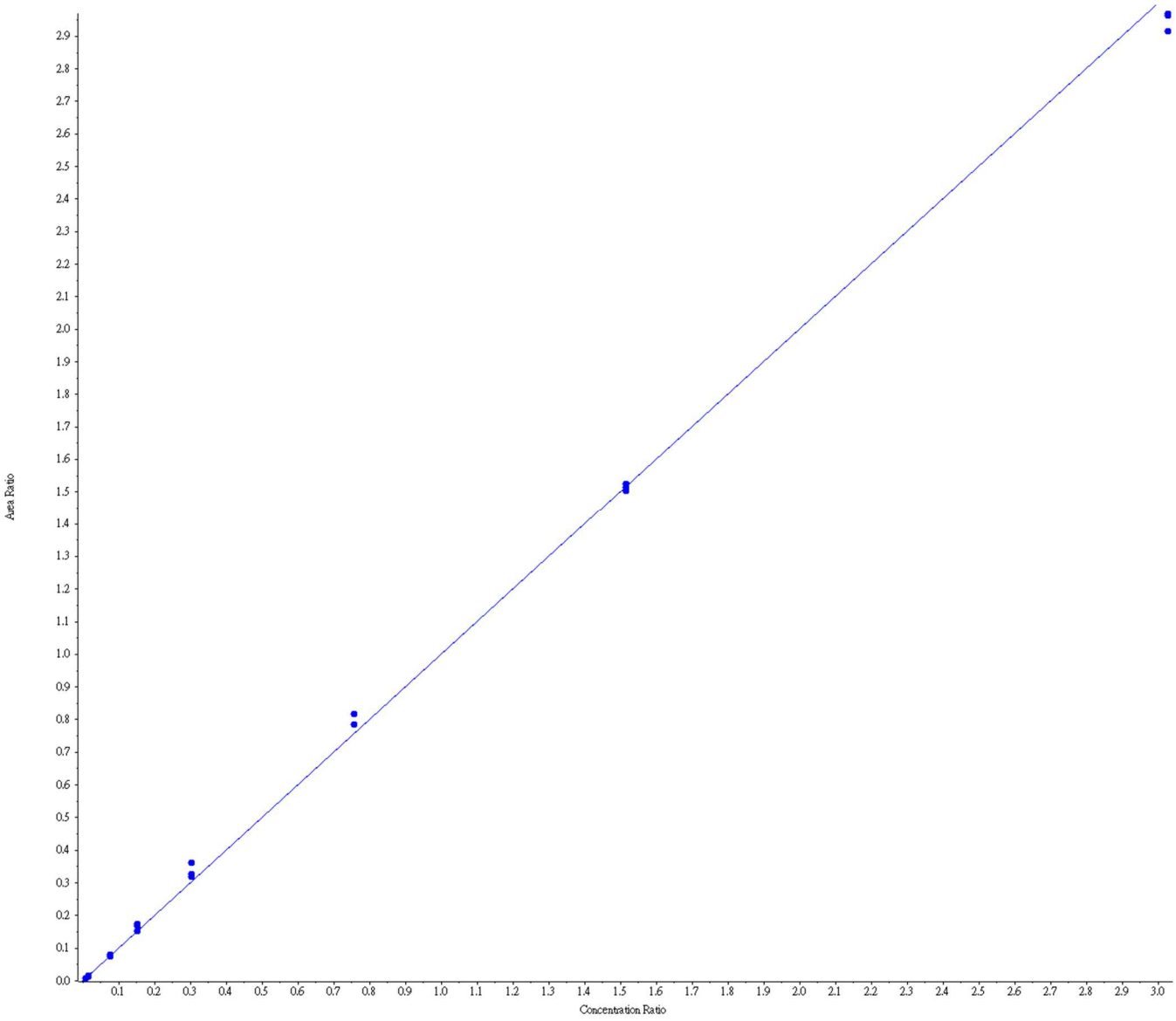
Analyte Name: **TSP1.FVFGTTPEDILR.2/y6.M00**

Calibration Equation: y = 1.04416 x + -0.00372 (r = 0.99609) (weighting: 1 / x)



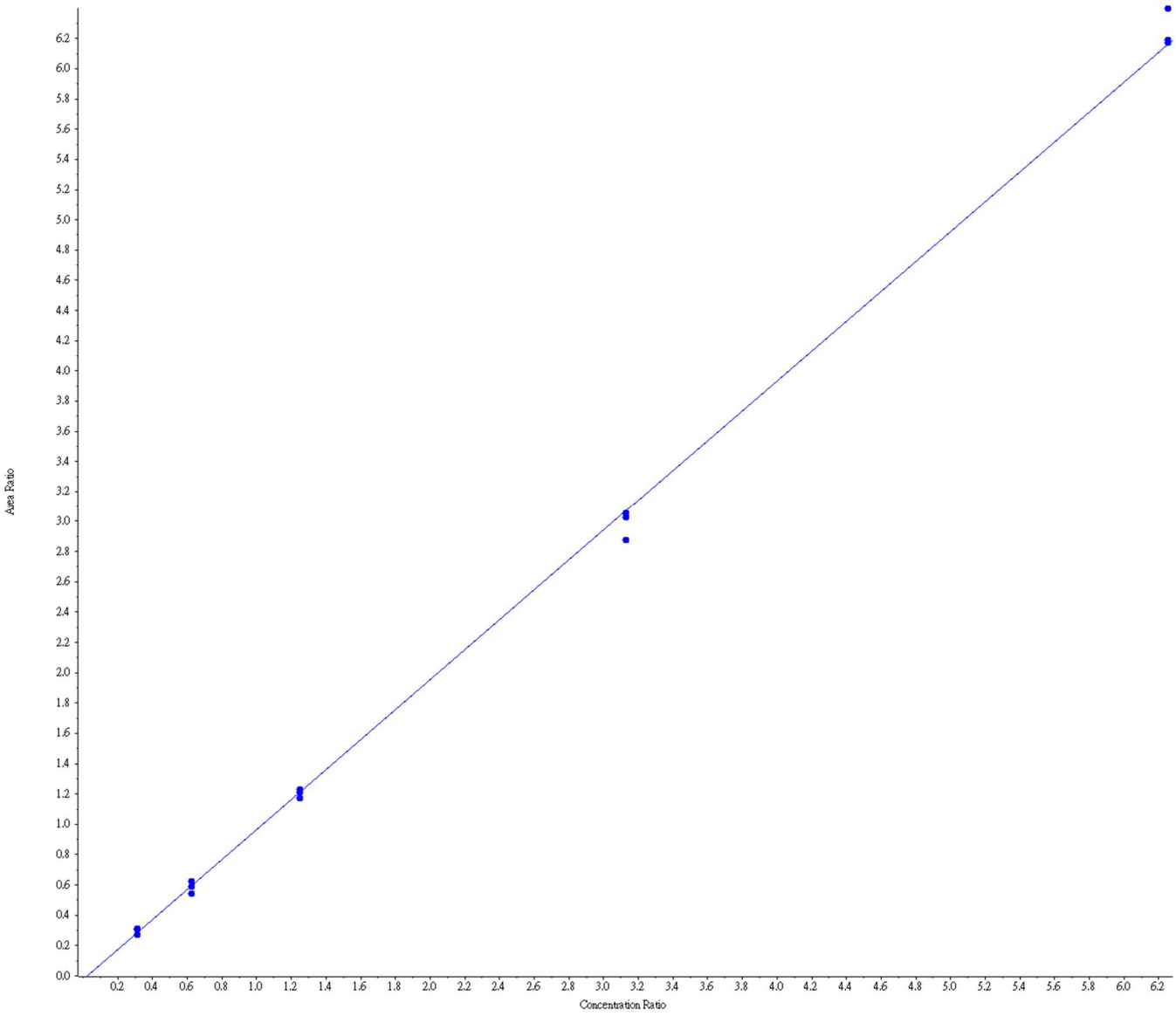
Analyte Name: **TRFE.EGYYGYTGAFR.2/y7.M00**

Calibration Equation: y = 1.00030 x + 0.00117 (r = 0.99900) (weighting: 1 / x)



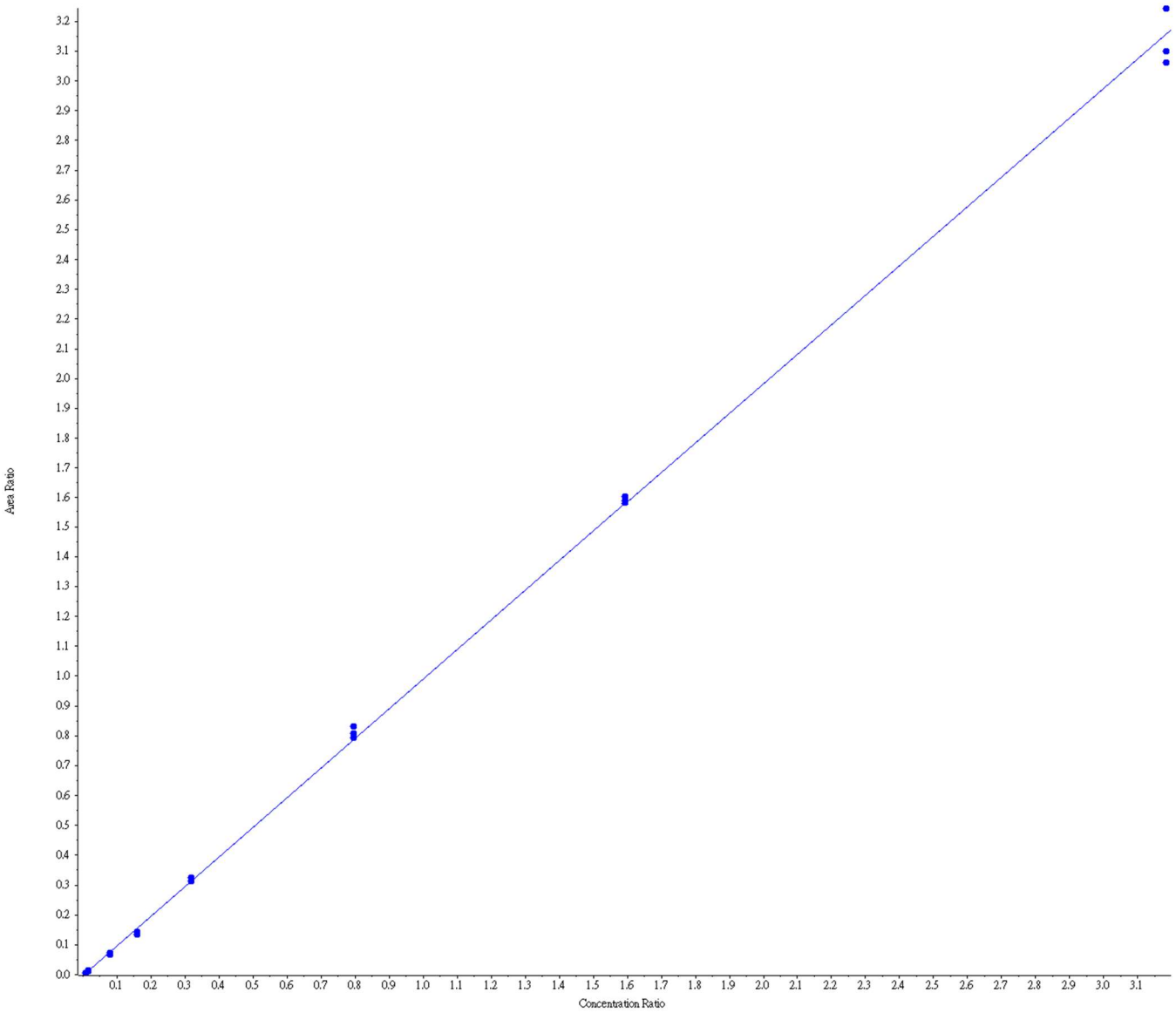
Analyte Name: **A1AG1.NWGLSVYADKPETTK.3/y13(2+).M00**

Calibration Equation: y = 0.98917 x + -0.02385 (r = 0.99924) (weighting: 1 / x)



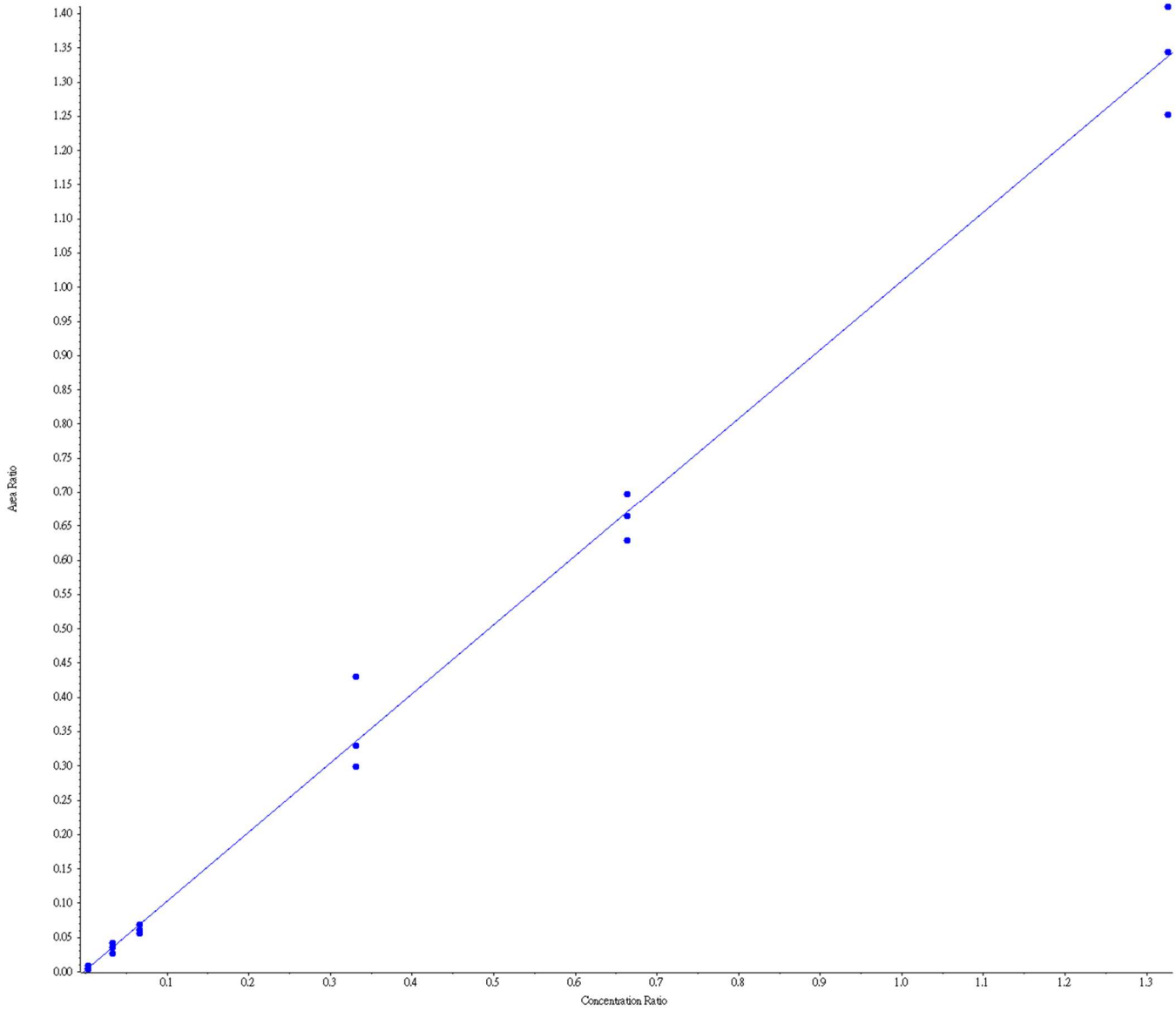
Analyte Name: **A2MG.TEHPFTVEEFVLPK.3/y6.M00**

Calibration Equation: y = 0.99264 x + -0.00285 (r = 0.99945) (weighting: 1 / x)



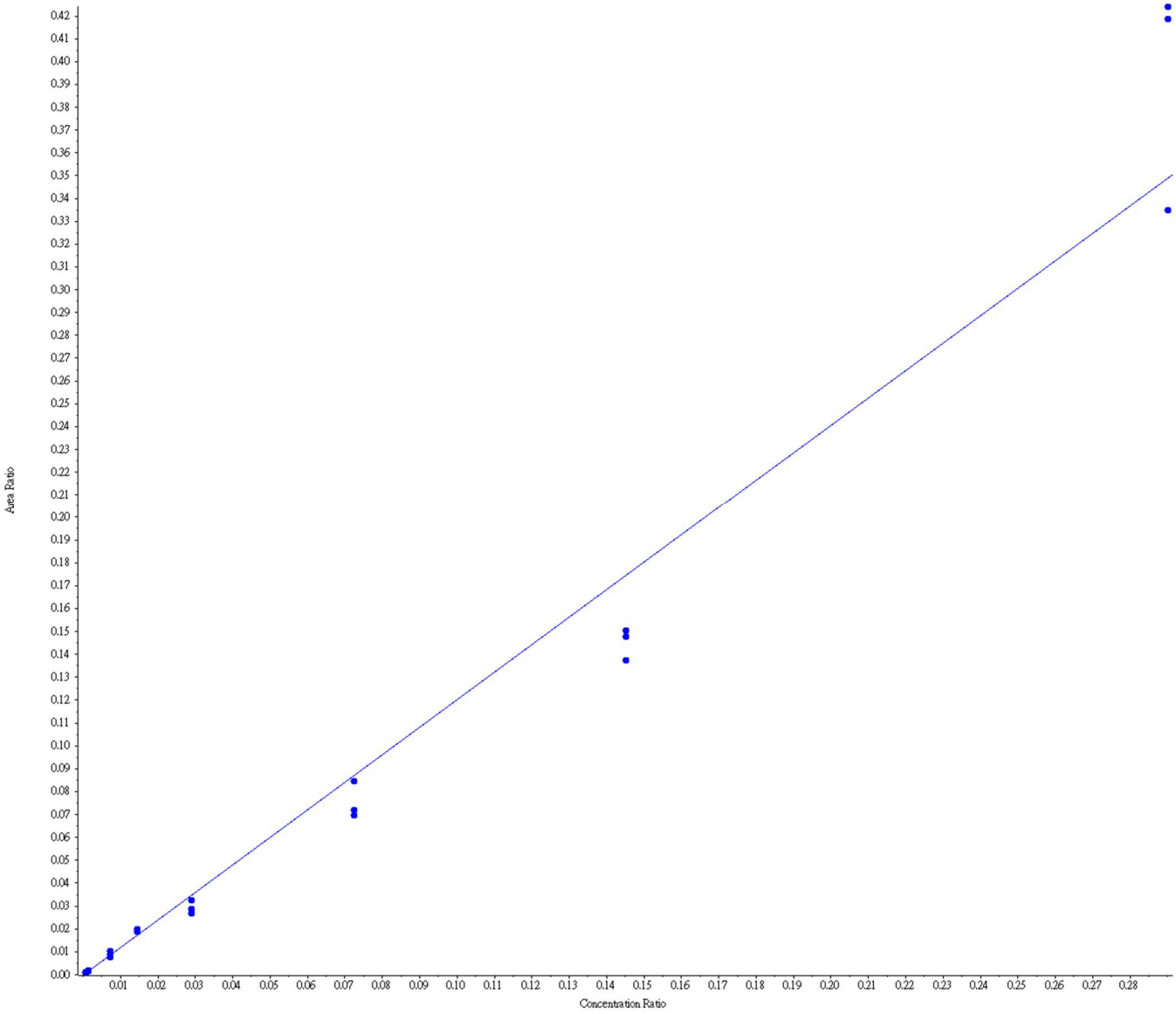
Analyte Name: **ANT3.DDLYVSDAFHK.2/y6.M00**

Calibration Equation: y = 1.00689 x + 0.00240 (r = 0.99613) (weighting: 1 / x)



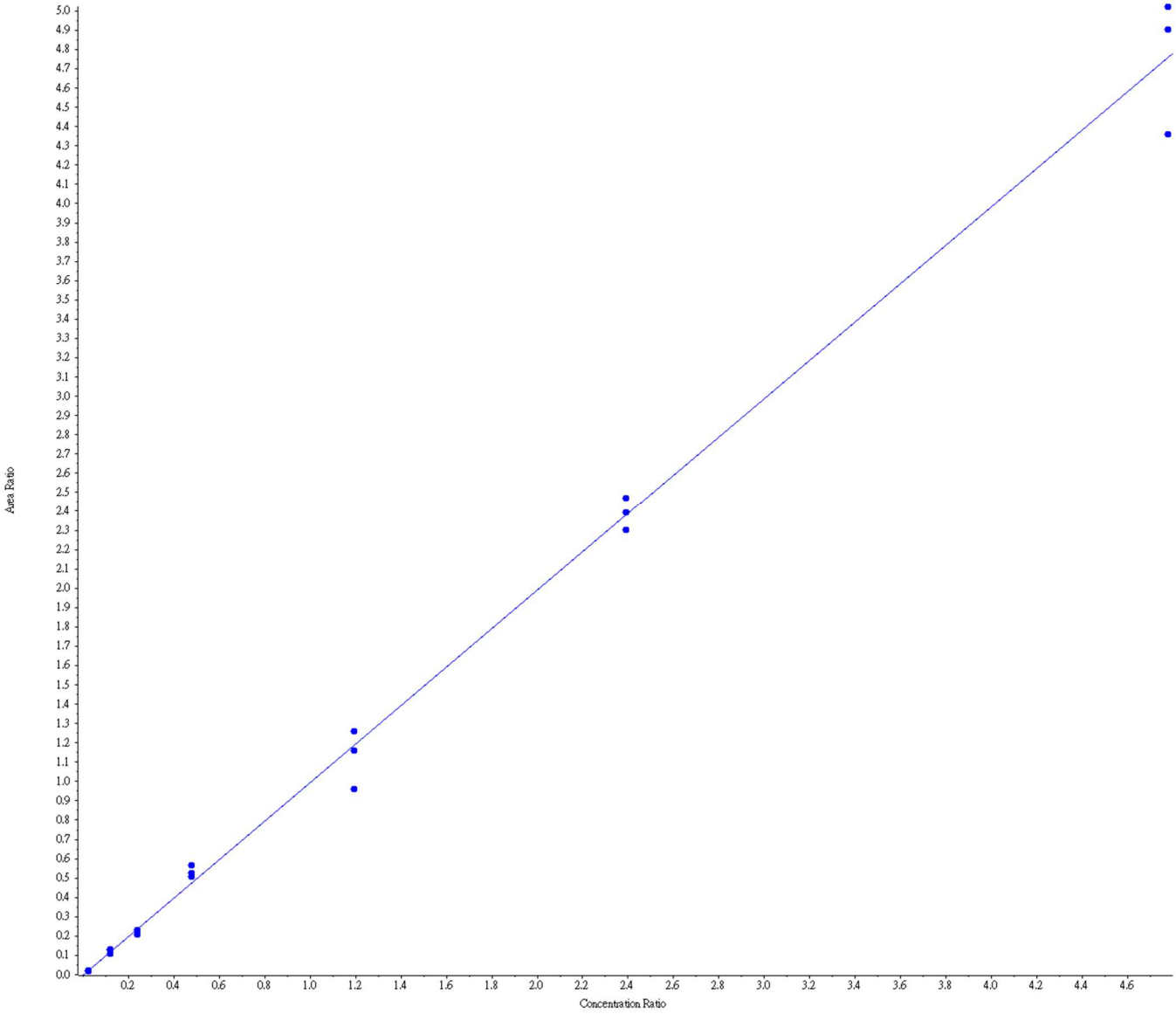
Analyte Name: **APOB.FPEVDVLTK.2/y8(2+).M00**

Calibration Equation: y = 1.20324 x + -1.46867e-4 (r = 0.98558) (weighting: 1 / x)



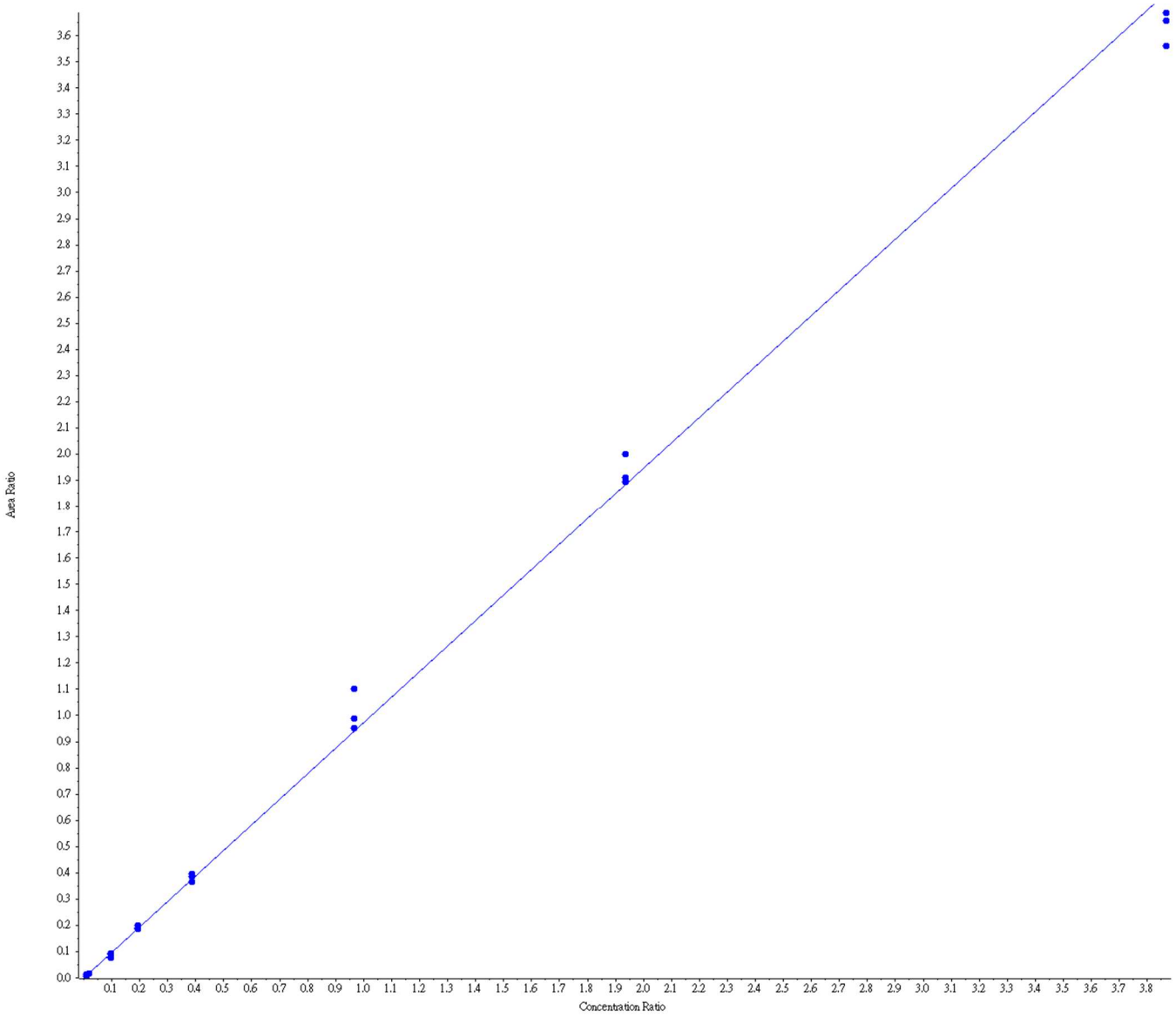
Analyte Name: **CERU.EYTDASFTNR.2/y4.M00**

Calibration Equation: y = 0.99644 x + -0.00190 (r = 0.99721) (weighting: 1 / x)



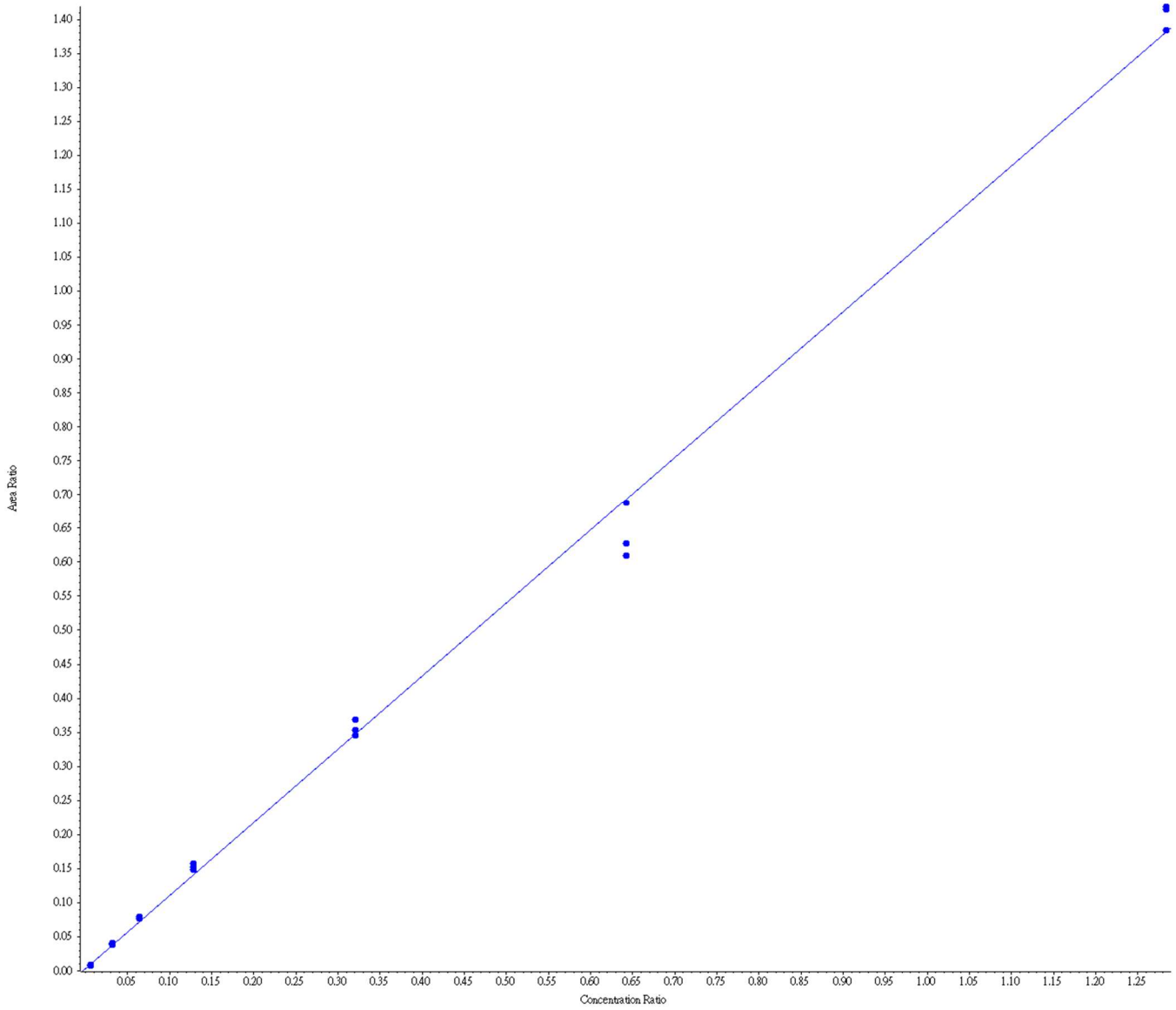
Analyte Name: **FIBA.GSESGIFTNTK.2/y5.M00**

Calibration Equation: y = 0.97316 x + -4.80402e-4 (r = 0.99853) (weighting: 1 / x)



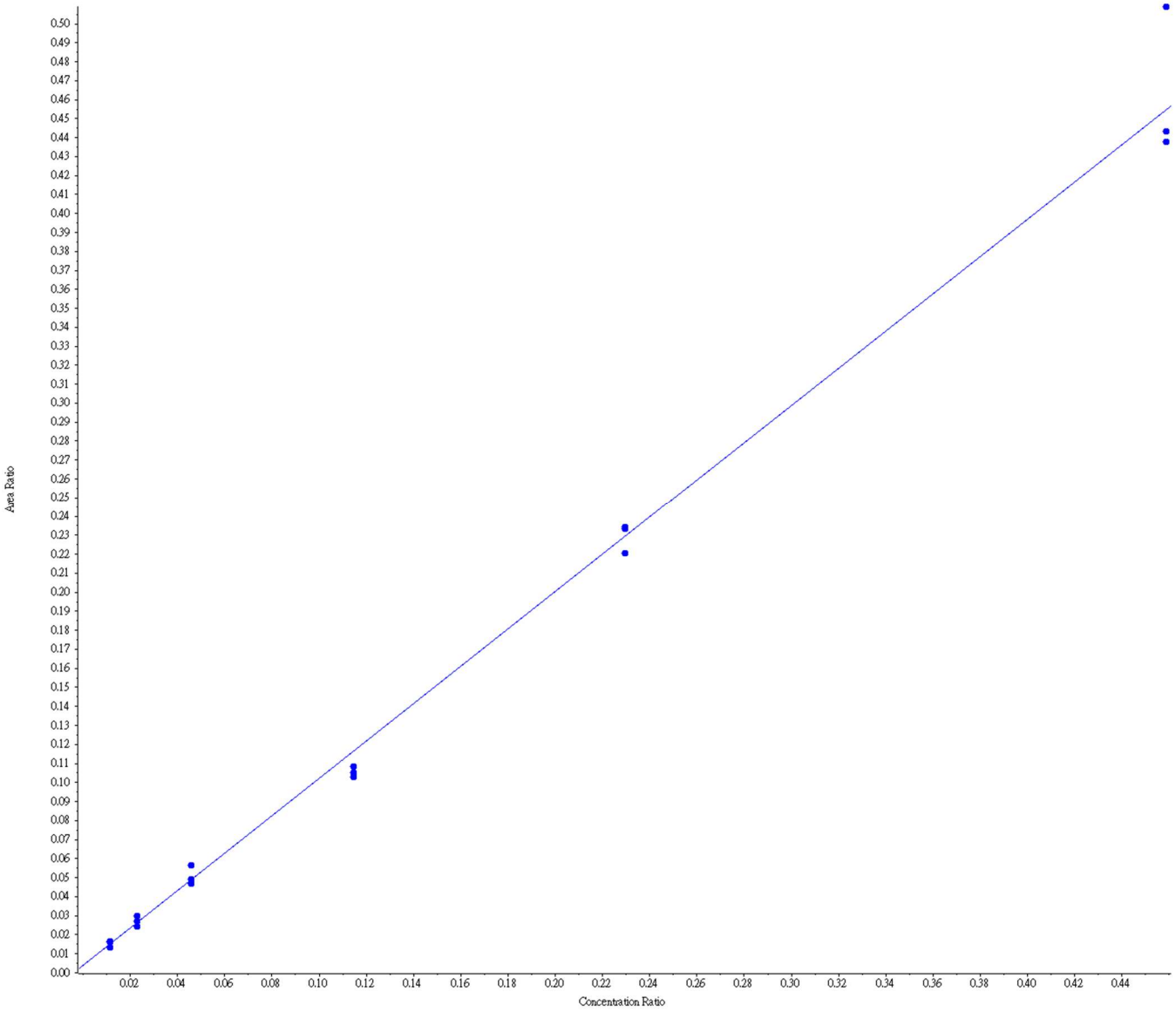
Analyte Name: **FIBG.DTVQIHDITGK.3/y9(2+).M00**

Calibration Equation: y = 1.07379 x + 0.00320 (r = 0.99827) (weighting: 1 / x)



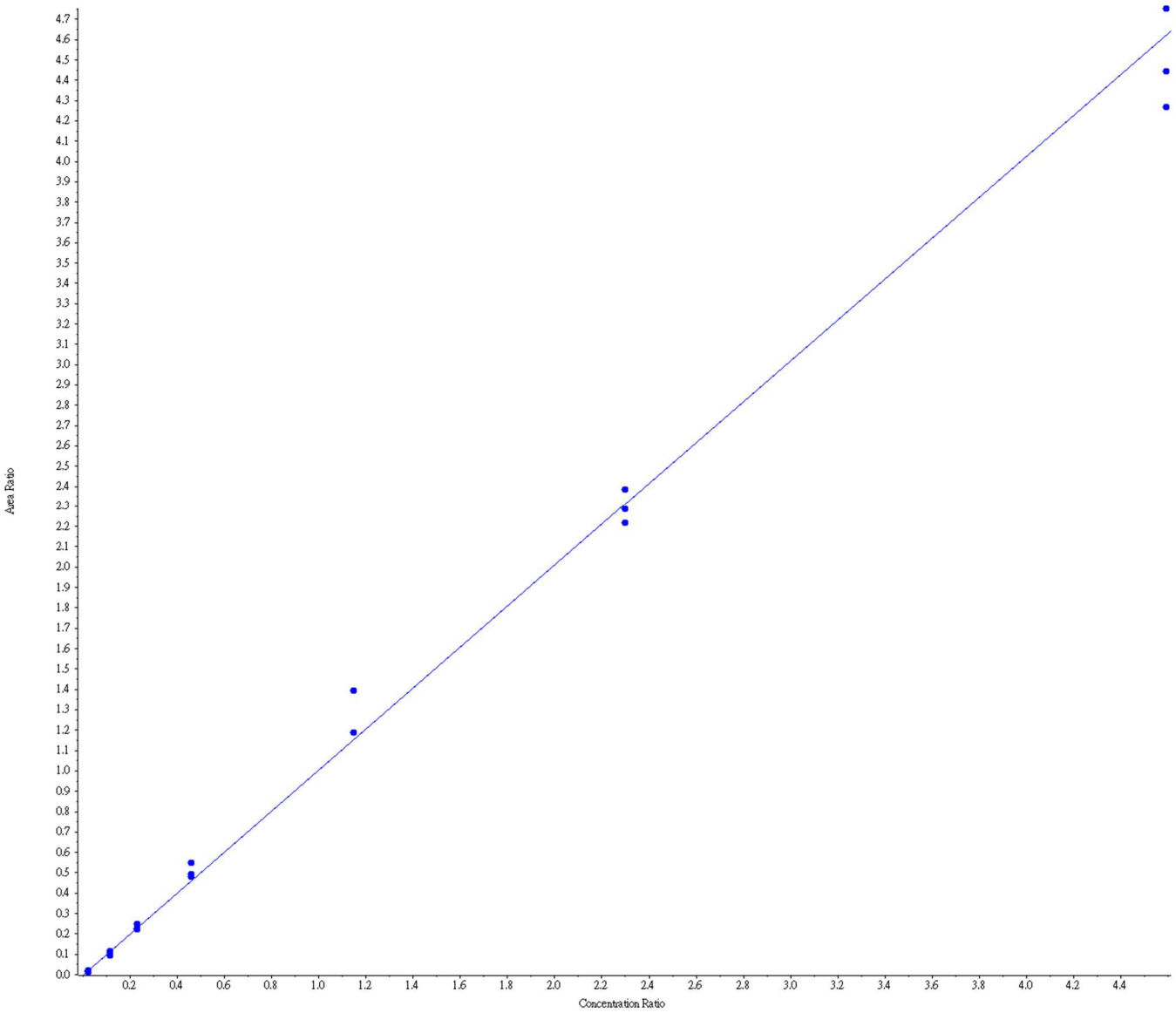
Analyte Name: **HEP2.TLEAQLTPR.2/y7.M00**

Calibration Equation: y = 0.98267 x + 0.00393 (r = 0.99640) (weighting: 1 / x)



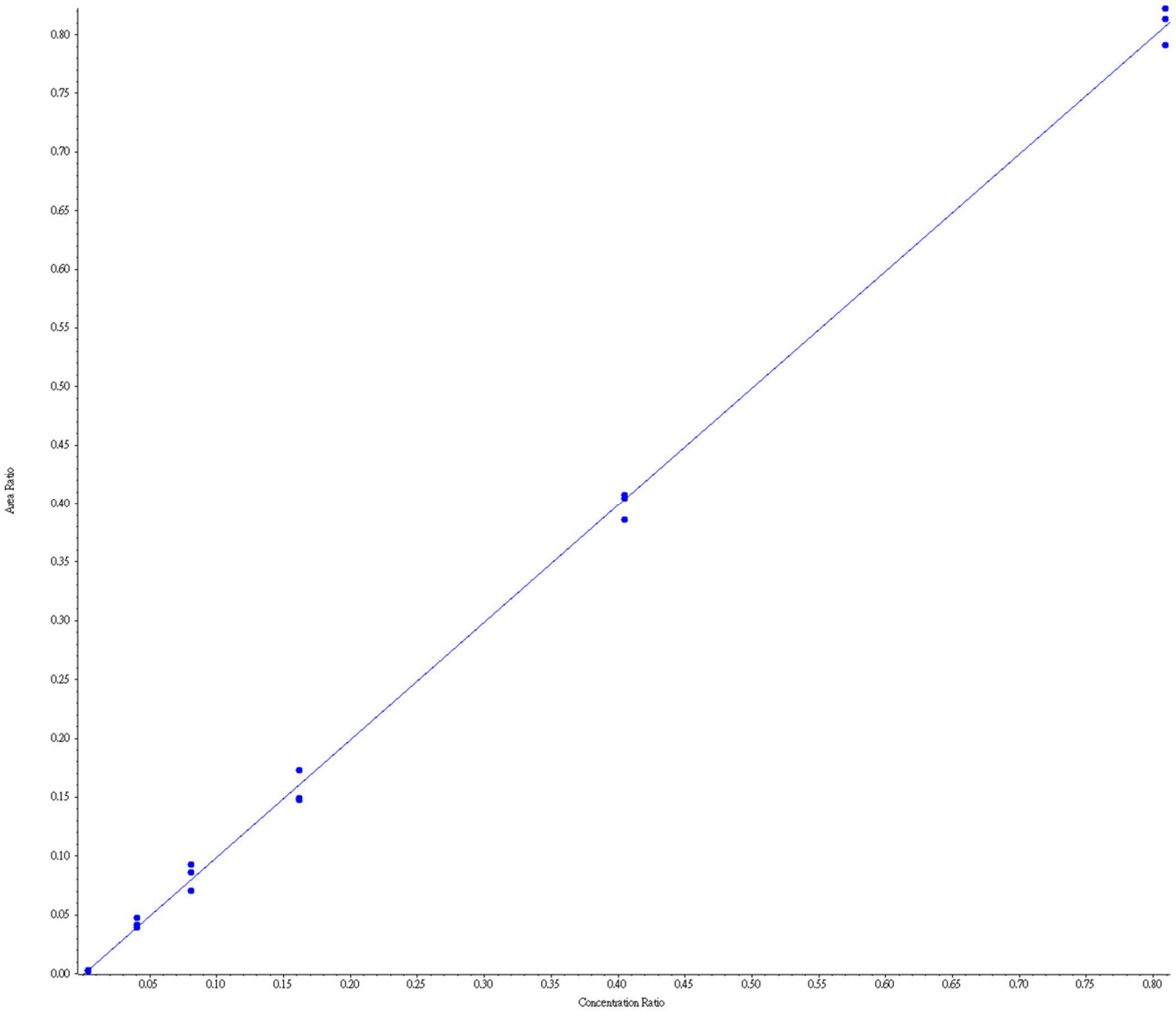
Analyte Name: **TTHY.AADDTWEPFASGK.2/y8.M00**

Calibration Equation: y = 1.00698 x + -0.00256 (r = 0.99748) (weighting: 1 / x)



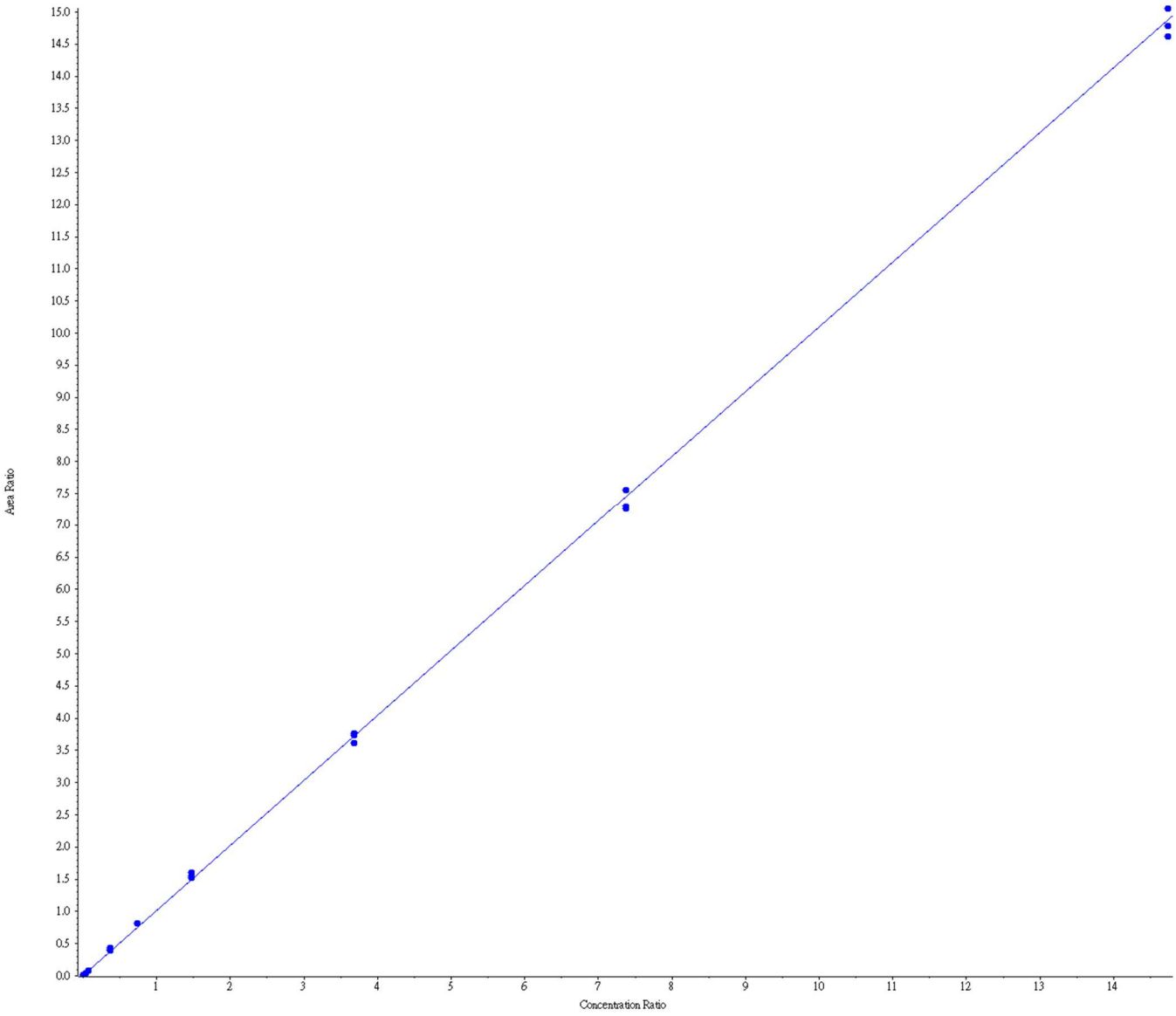
Analyte Name: **VTDB.THLPEVFLSK.2/y8.M00**

Calibration Equation: y = 0.99901 x + -9.81721e-4 (r = 0.99881) (weighting: 1 / x)



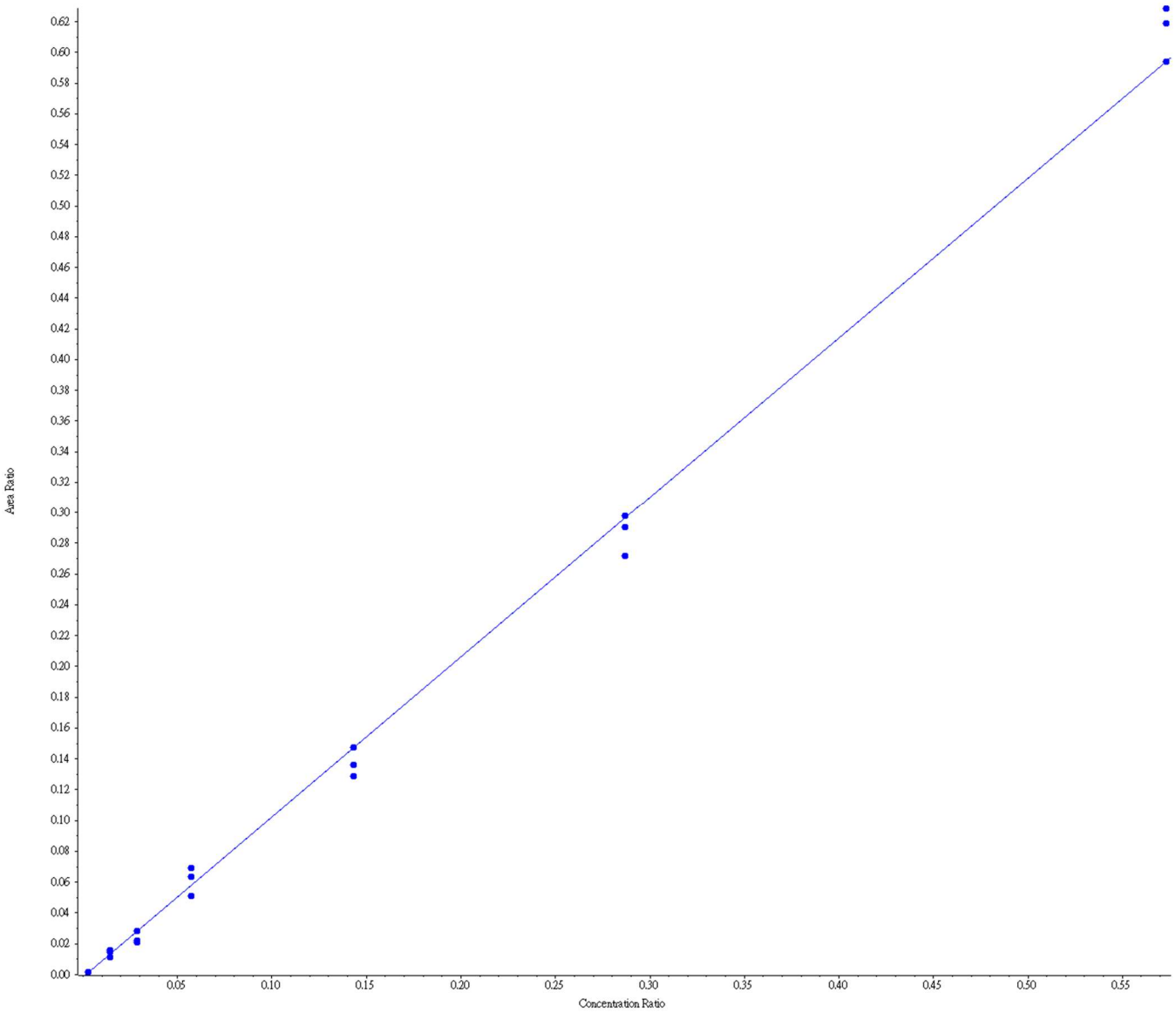
Analyte Name: **ALBU.LVNEVTEFAK.2/y5.M00**

Calibration Equation: y = 1.00903 x + 0.00786 (r = 0.99967) (weighting: 1 / x)



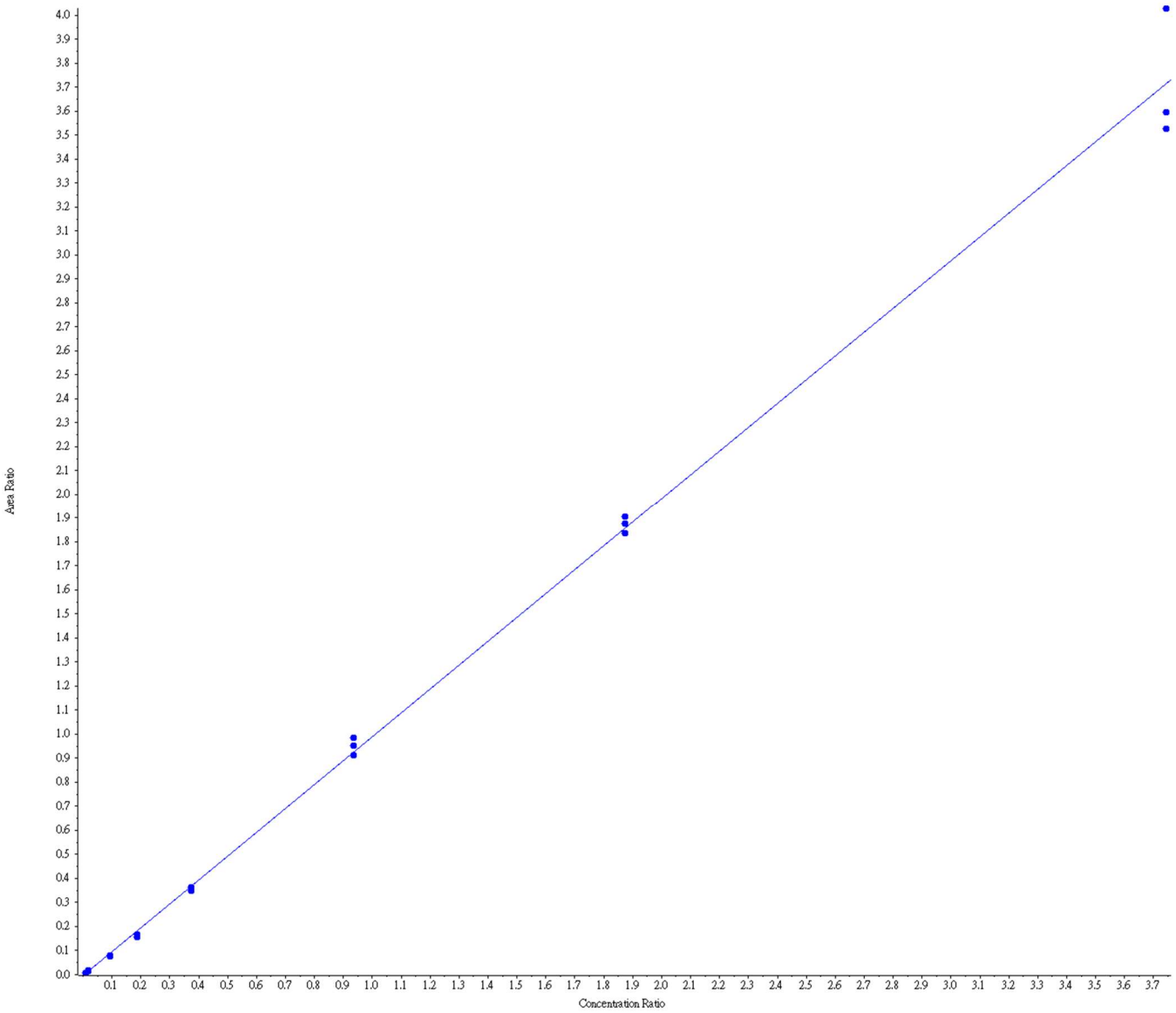
Analyte Name: **AACT.EIGELYLPK.2/y5.M00**

Calibration Equation: y = 1.03910 x + -0.00151 (r = 0.99752) (weighting: 1 / x)



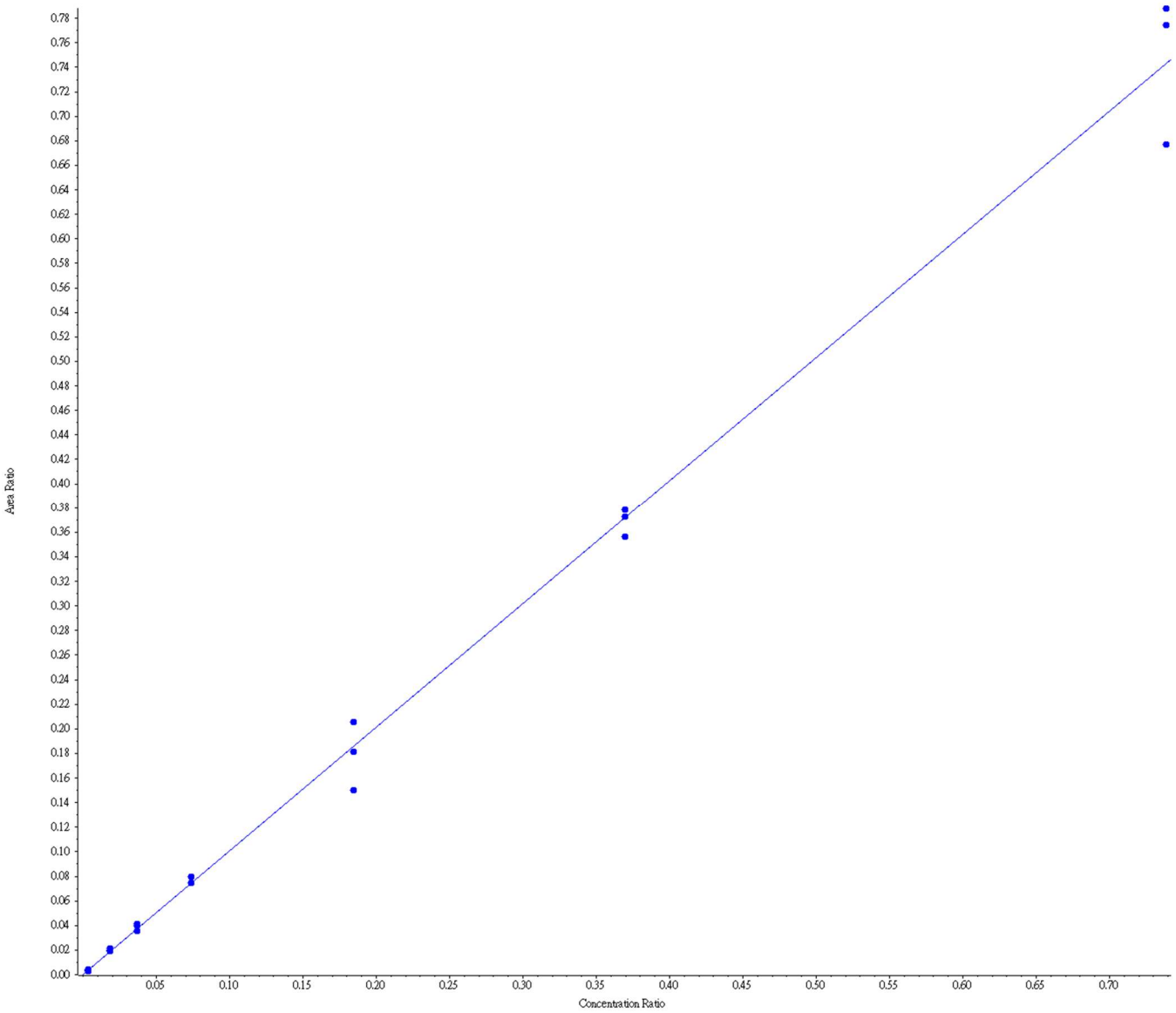
Analyte Name: **A1BG.LETPDFQLFK.2/y7.M00**

Calibration Equation: y = 0.99343 x + -0.00367 (r = 0.99854) (weighting: 1 / x)



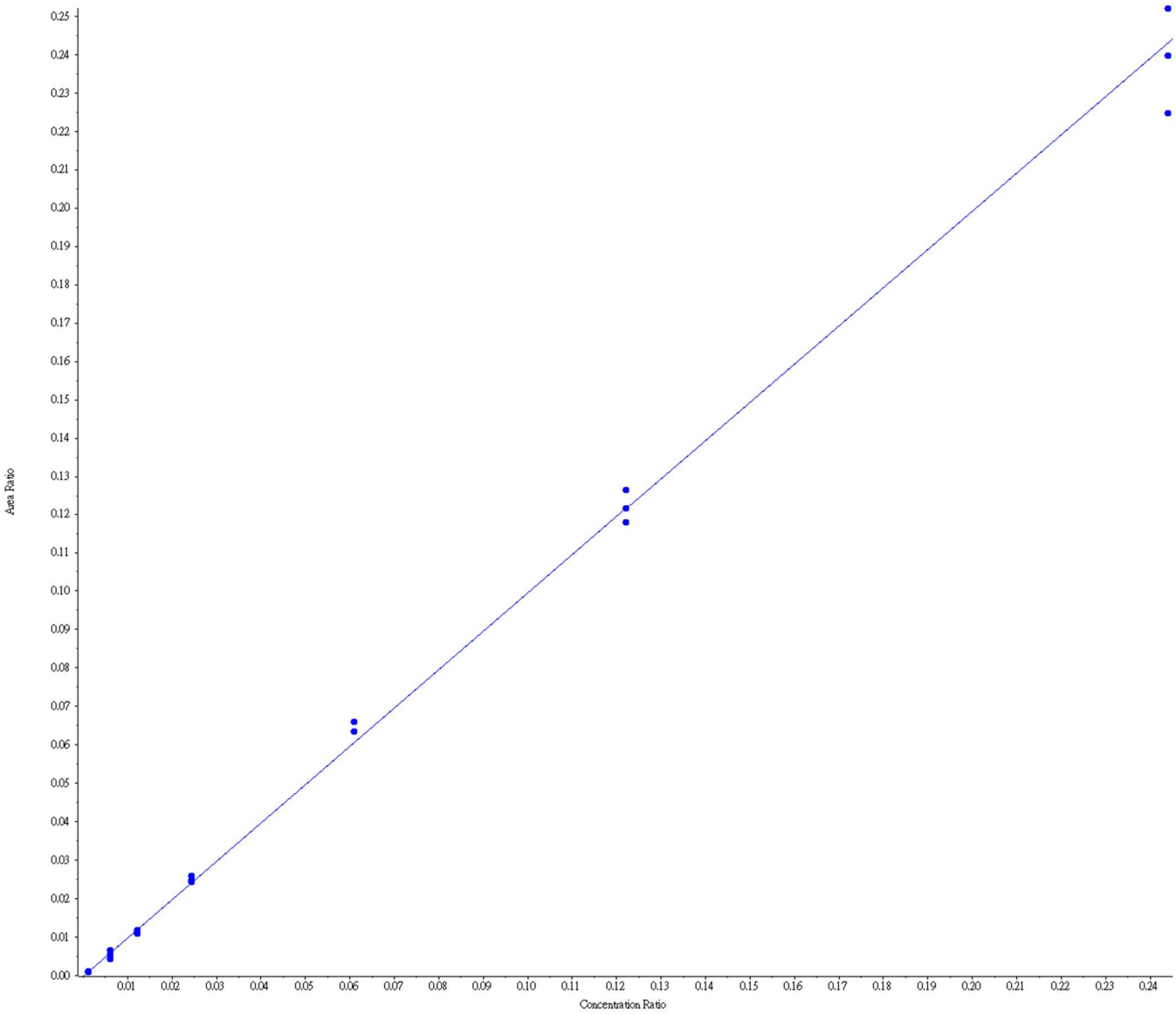
Analyte Name: **APOC1.TPDVSSALDK.2/y6.M00**

Calibration Equation: y = 1.00584 x + 2.10769e-4 (r = 0.99723) (weighting: 1 / x)



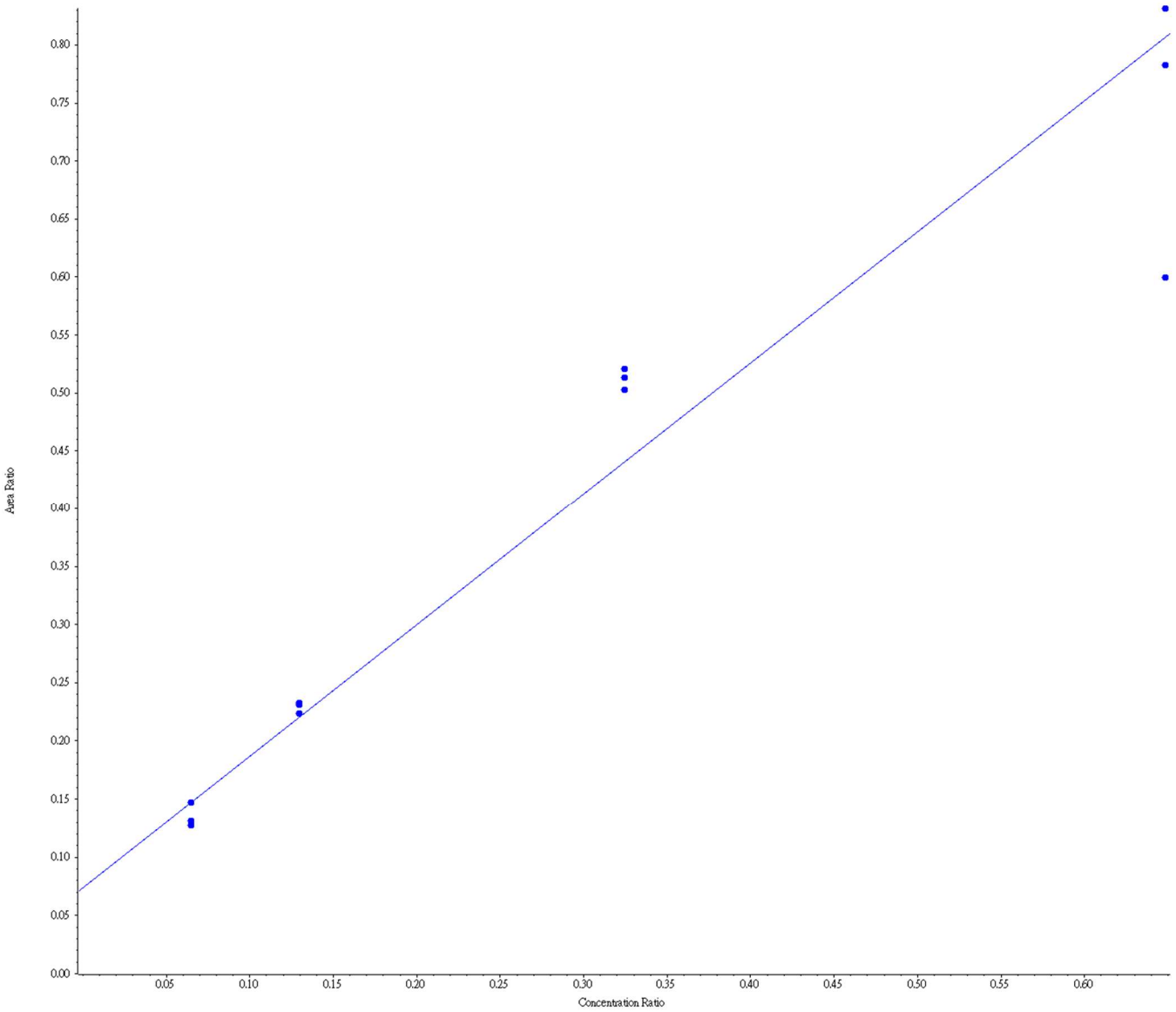
Analyte Name: **APOC3.GWVTDGFSSLK.2/y8.M00**

Calibration Equation: y = 0.99715 x + -2.08728e-4 (r = 0.99858) (weighting: 1 / x)



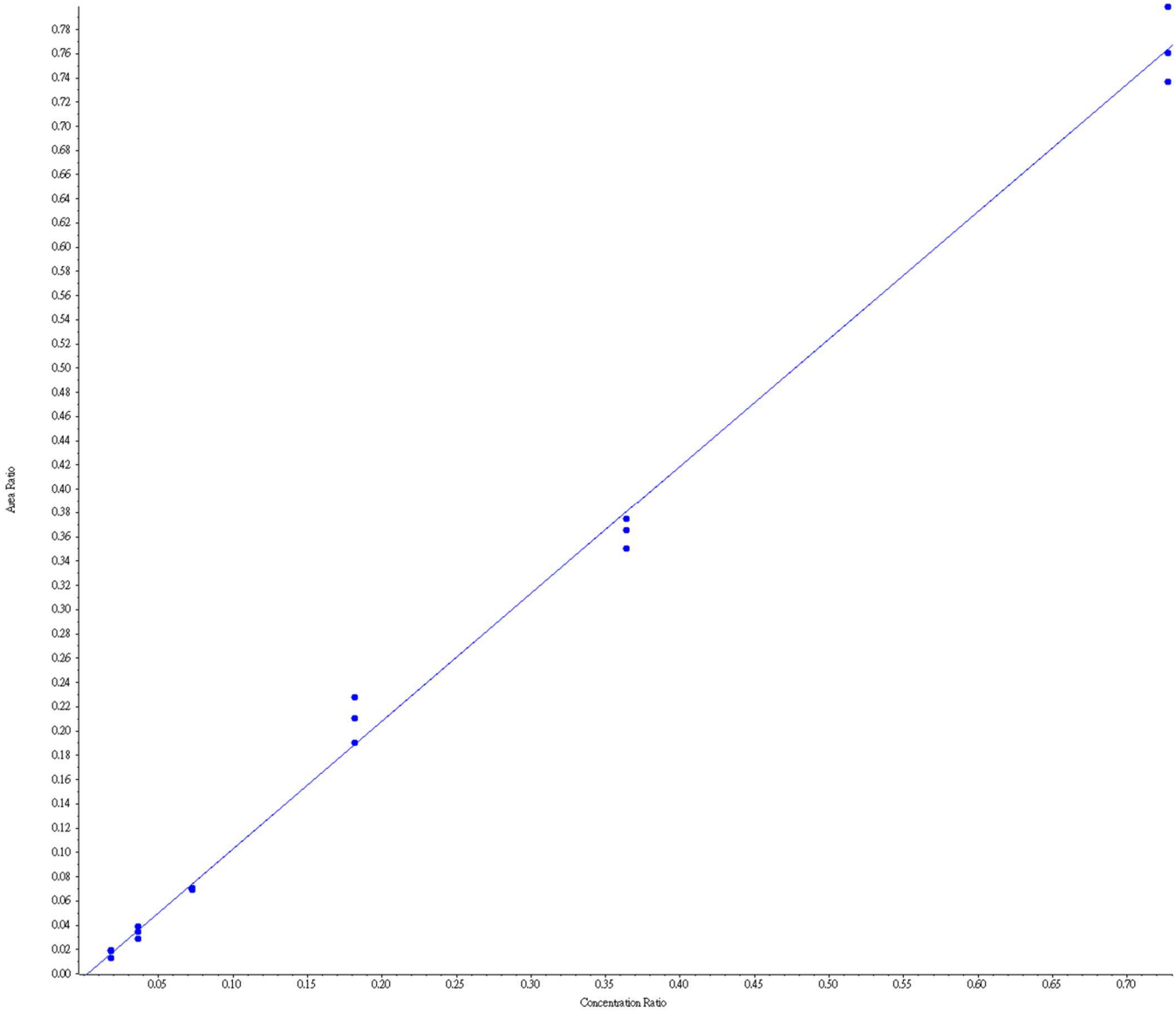
Analyte Name: **APOD.IPTTFENGR.2/y8(2+).M00**

Calibration Equation: y = 1.13007 x + 0.07386 (r = 0.97283) (weighting: 1 / x)



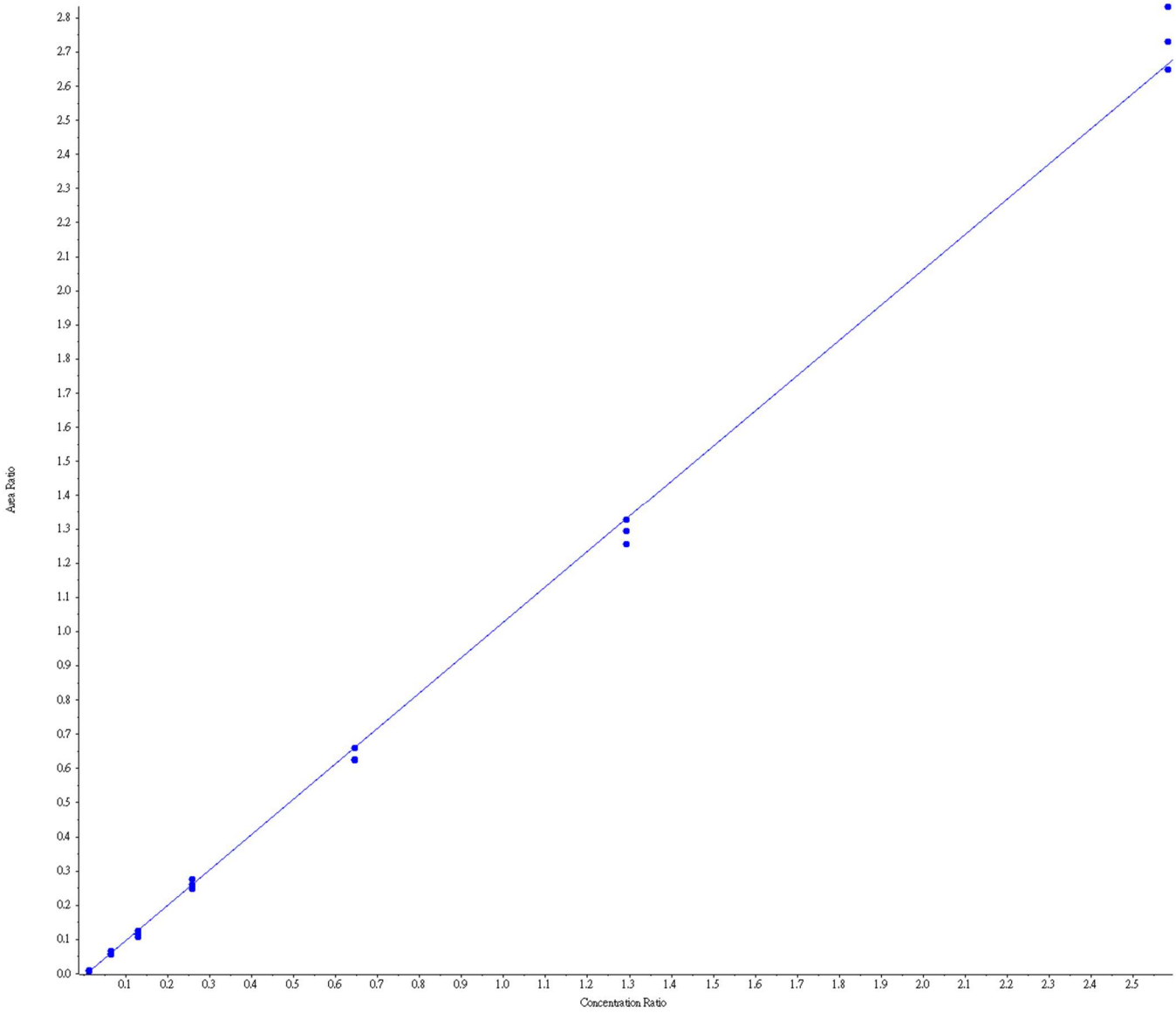
Analyte Name: **APOE.LGPLVEQGR.2/y7(2+).M00**

Calibration Equation: y = 1.05356 x + -0.00253 (r = 0.99707) (weighting: 1 / x)



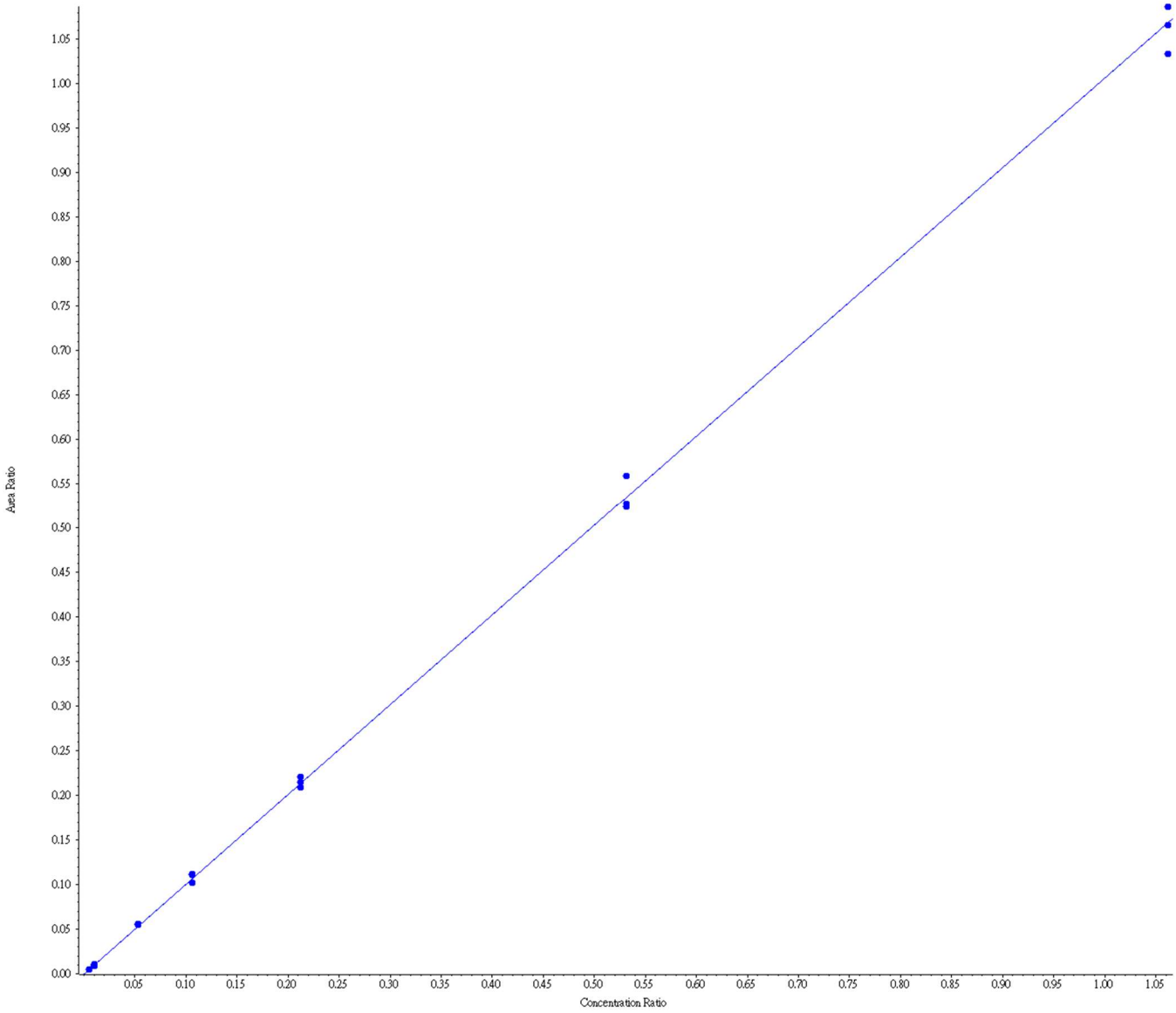
Analyte Name: **CLUS.ELDESLQVAER.2/y3.M00**

Calibration Equation: y = 1.03409 x + -0.00630 (r = 0.99897) (weighting: 1 / x)



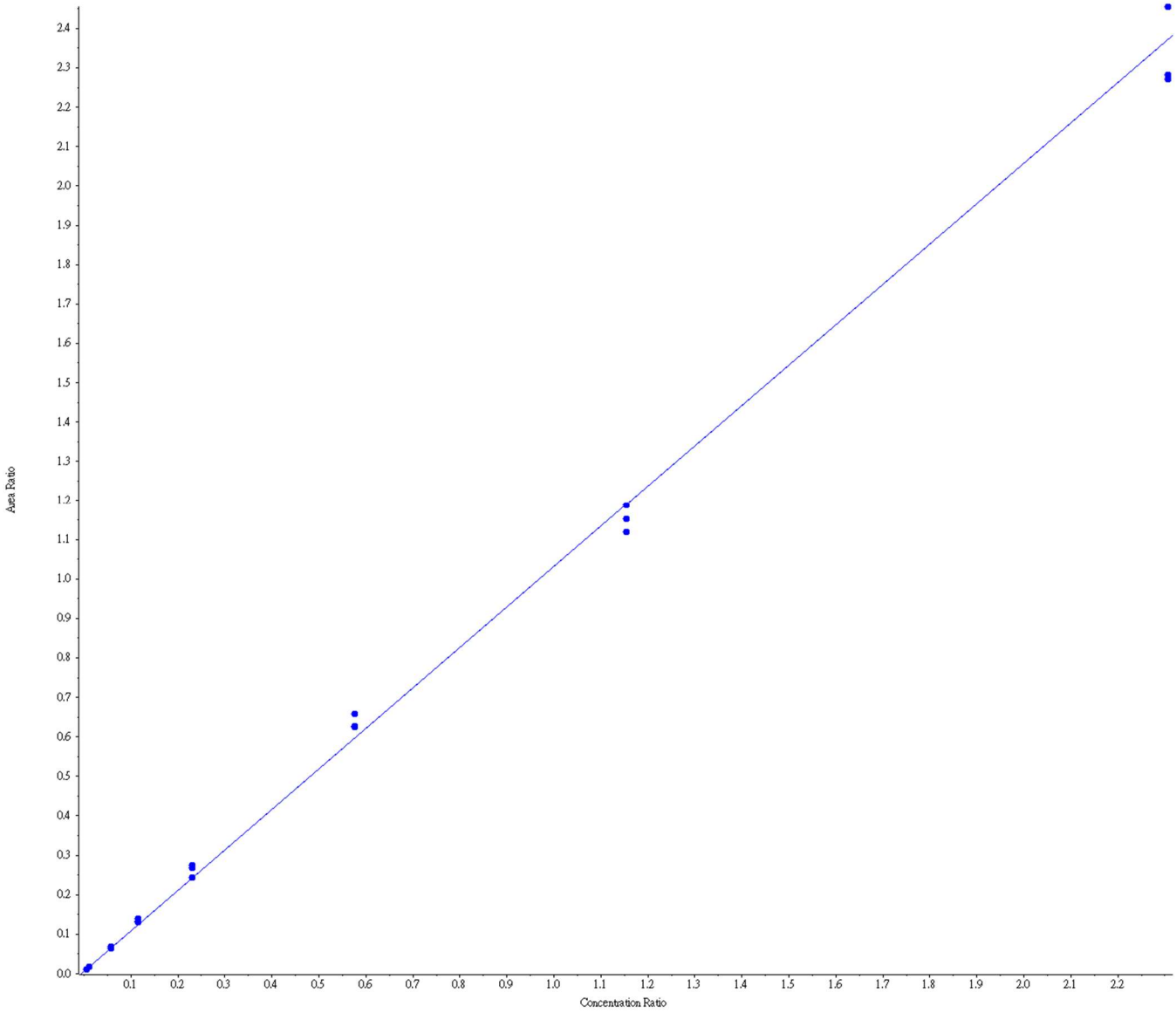
Analyte Name: **C1 inactivator.LLDSLPSDTR.2/y5.M00**

Calibration Equation: y = 1.00670 x + -3.85779e-4 (r = 0.99960) (weighting: 1 / x)



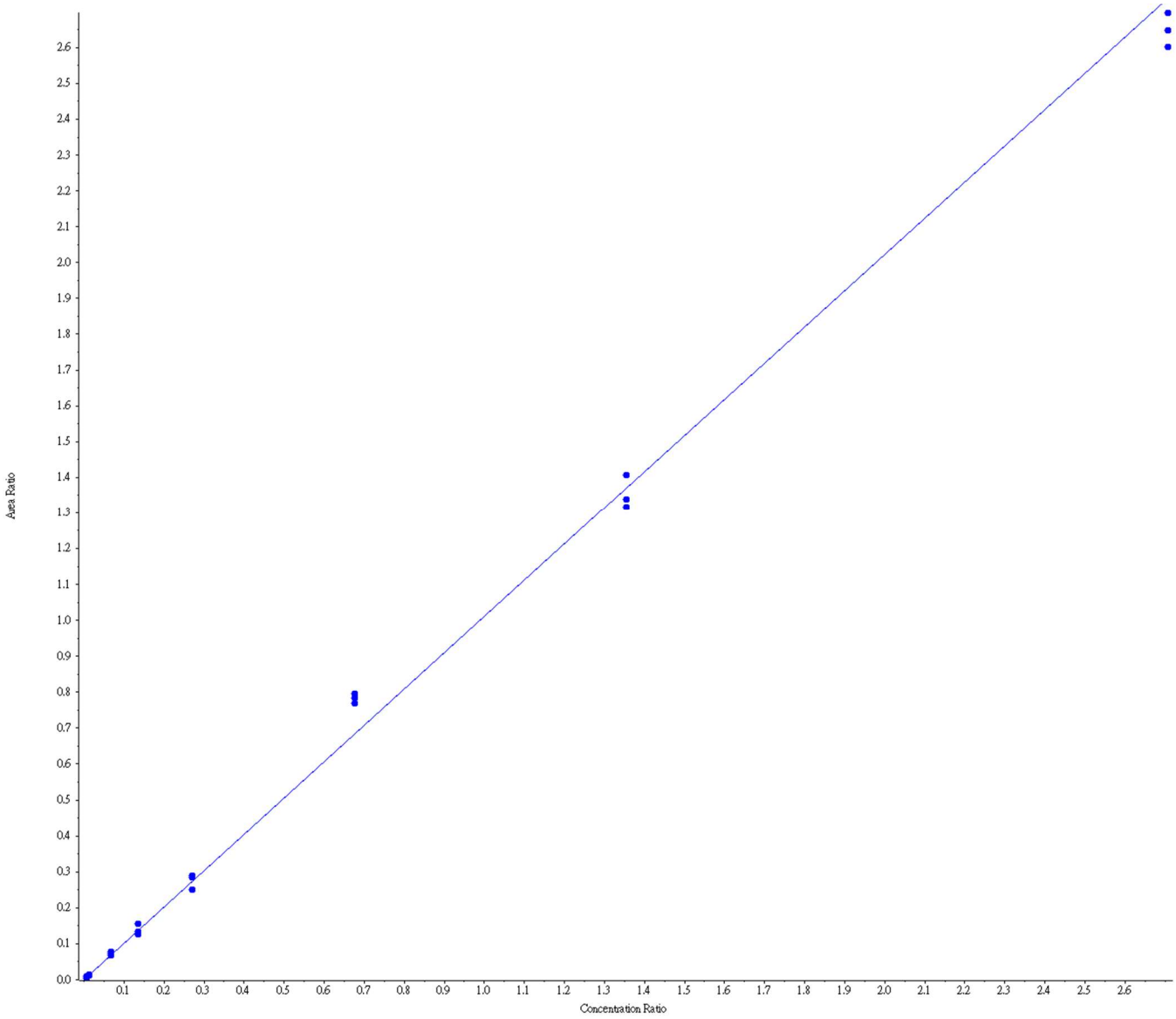
Analyte Name: **CFB.EELLPAQDIK.2/y6.M00**

Calibration Equation: y = 1.02584 x + 0.00595 (r = 0.99857) (weighting: 1 / x)



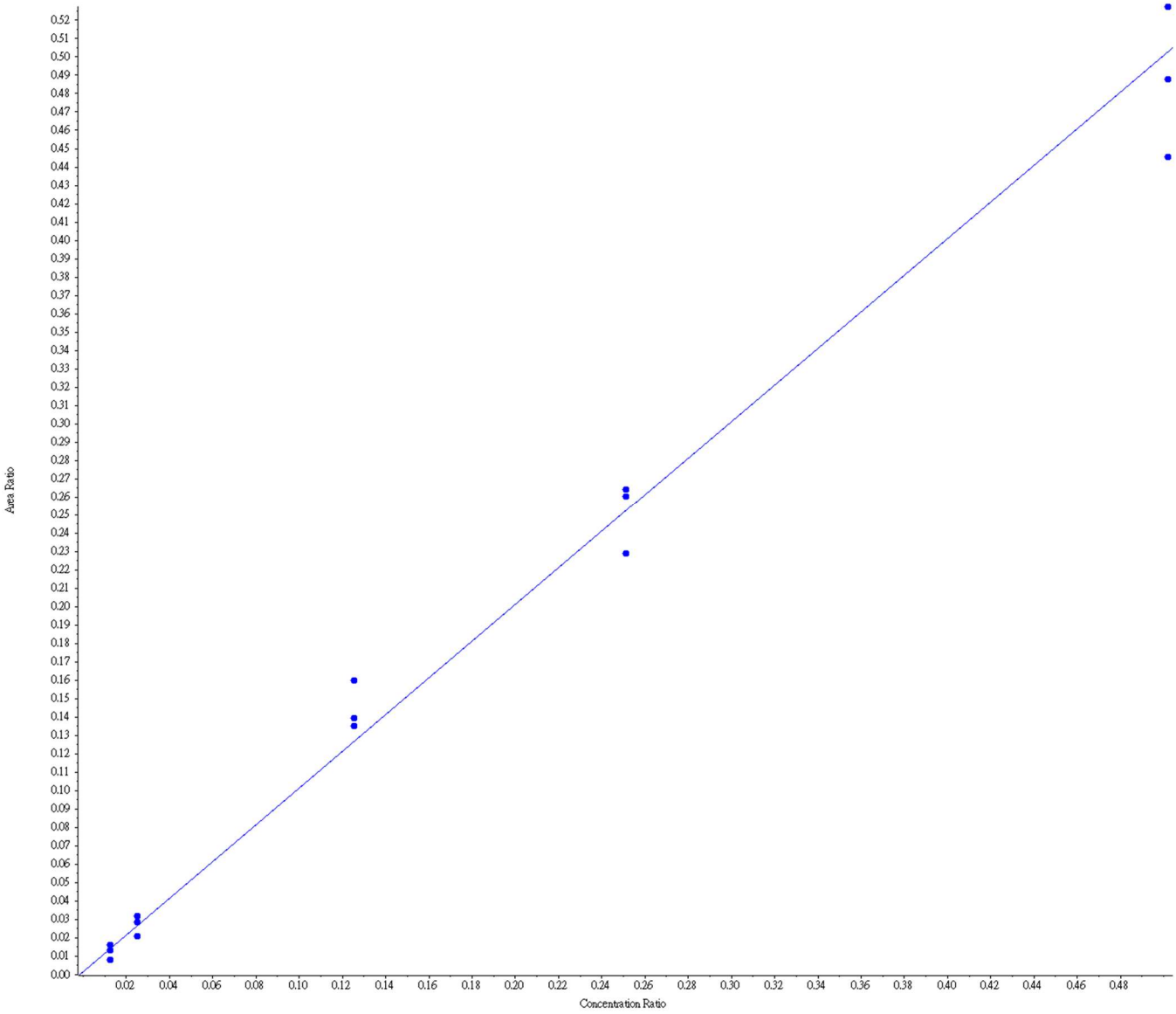
Analyte Name: **CFAH.SPDVINGSPISQK.2/y8.M00**

Calibration Equation: y = 1.01129 x + 5.77002e-5 (r = 0.99772) (weighting: 1 / x)



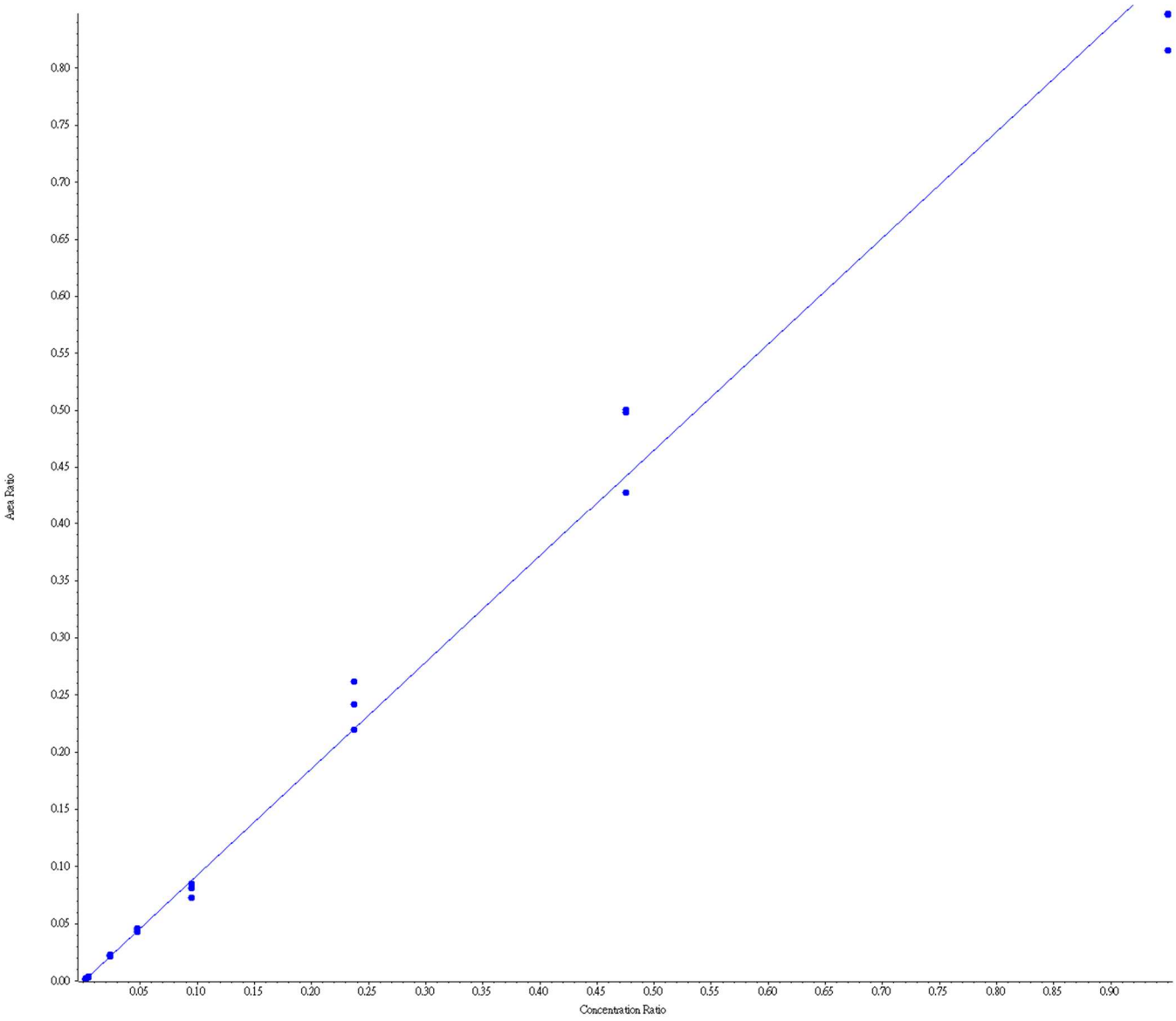
Analyte Name: **CRP.ESDTSYVSLK.2/y3.M00**

Calibration Equation: y = 0.99844 x + 0.00160 (r = 0.99374) (weighting: 1 / x)



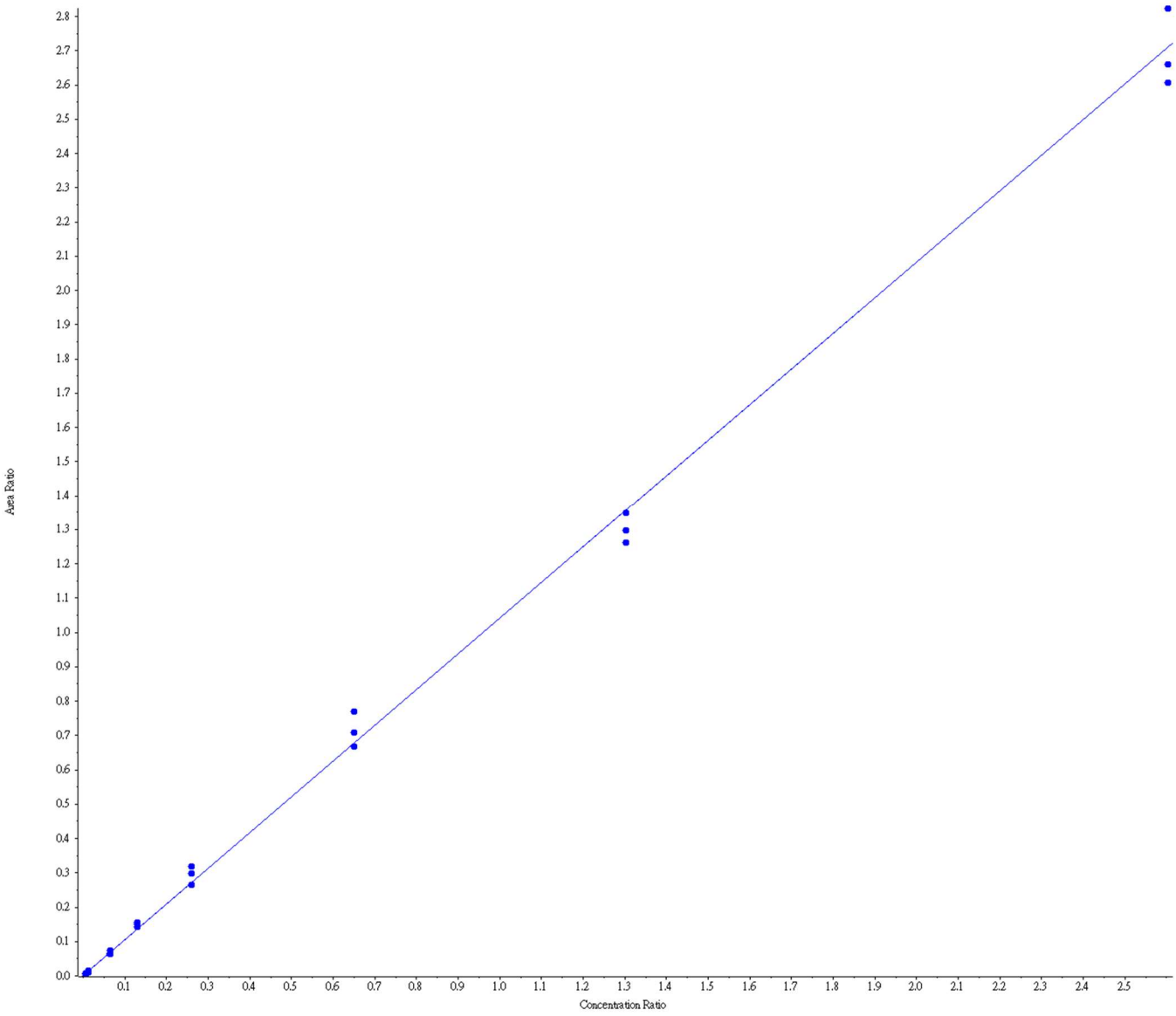
Analyte Name: **A2AP.LGNQEPGGQTALK.2/y8.M00**

Calibration Equation: y = 0.93131 x + -6.75118e-4 (r = 0.99619) (weighting: 1 / x)



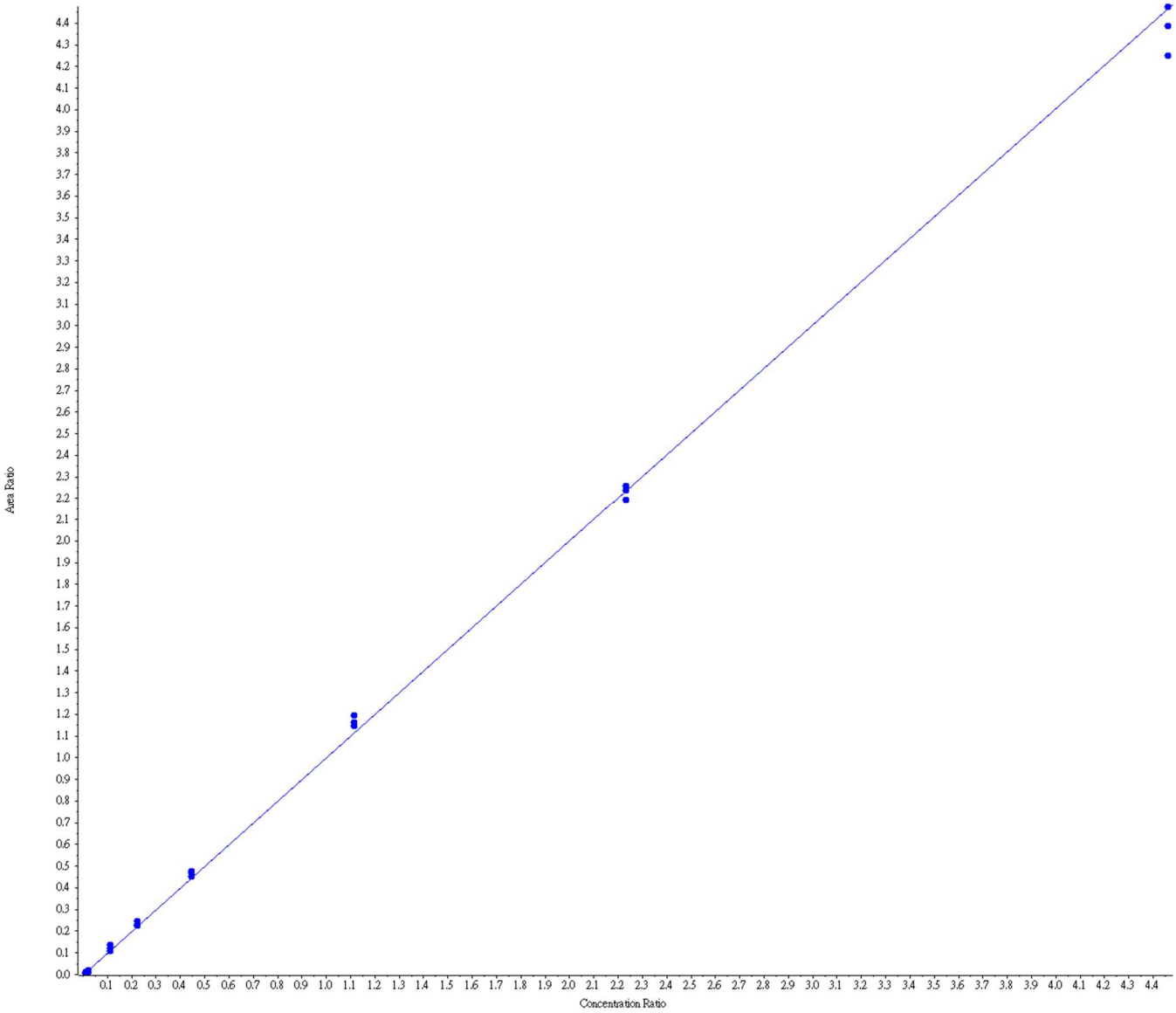
Analyte Name: **GELS.TGAQELLR.2/y5.M00**

Calibration Equation: y = 1.04104 x + 9.59314e-4 (r = 0.99834) (weighting: 1 / x)



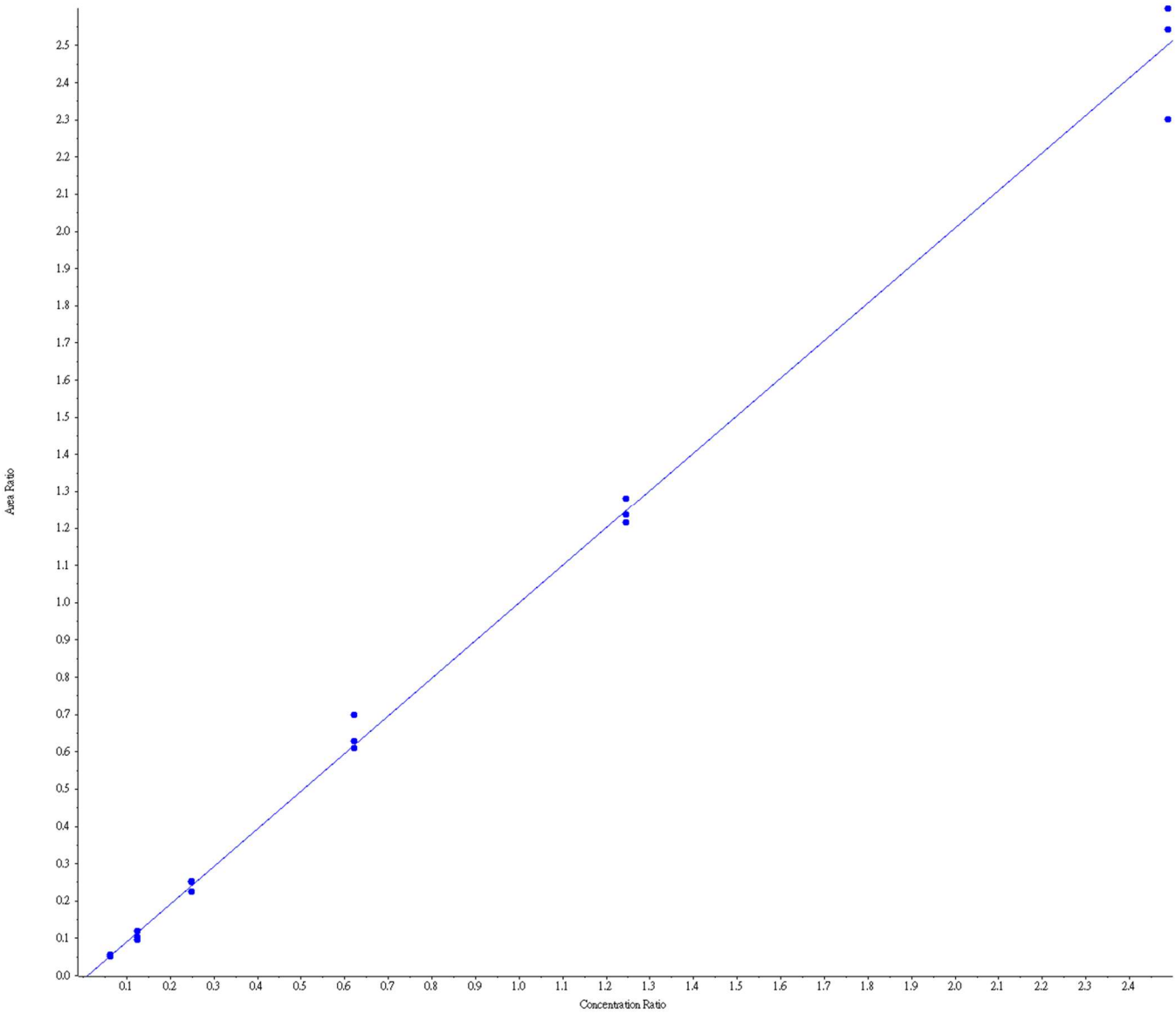
Analyte Name: **KNG1.TVGSDTFYSFK.2/y9.M00**

Calibration Equation: y = 1.00182 x + -0.00216 (r = 0.99914) (weighting: 1 / x)



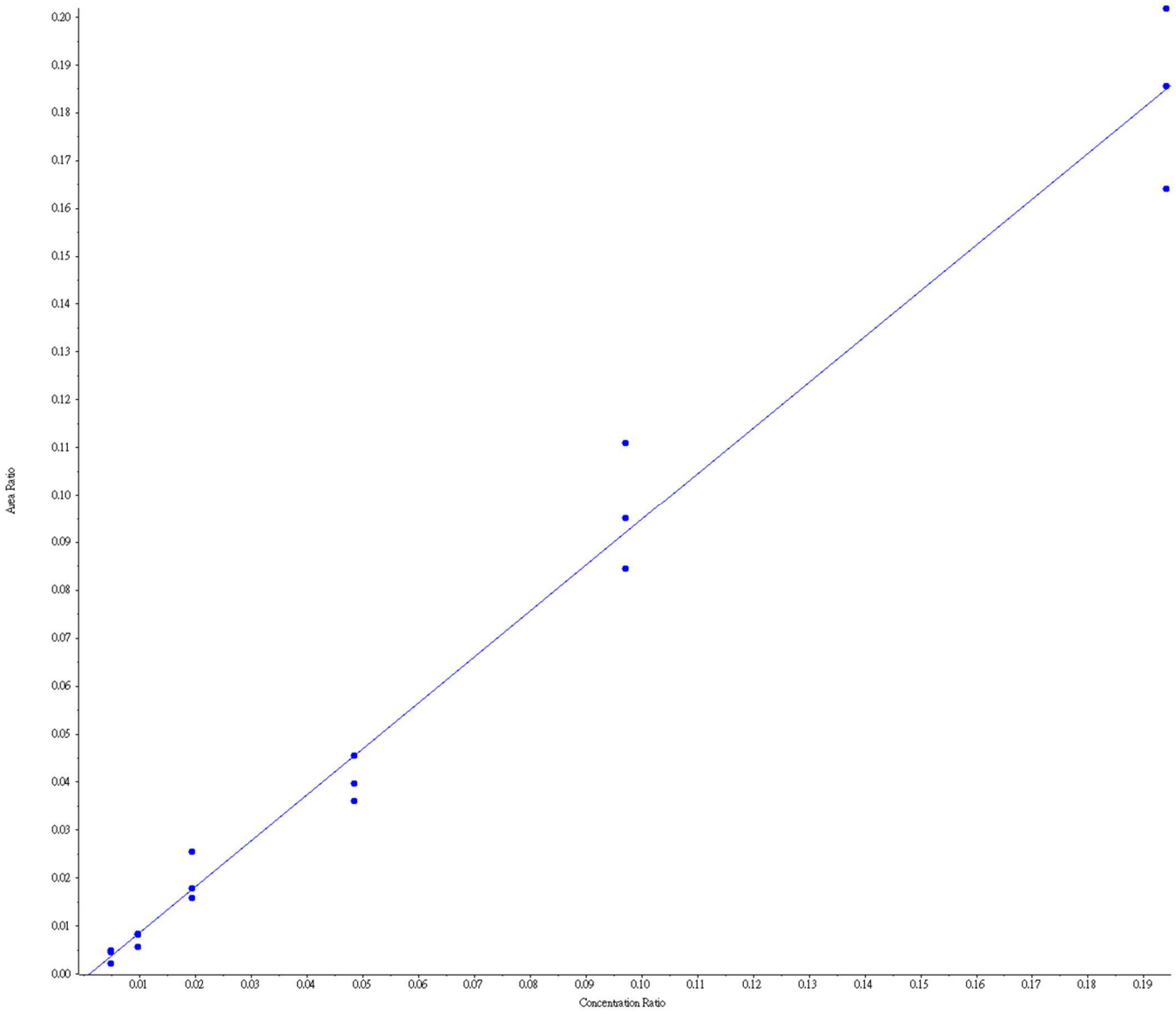
Analyte Name: **RBP.YWGVASFLQK.2/y8.M00**

Calibration Equation: y = 1.01000 x + -0.01037 (r = 0.99820) (weighting: 1 / x)



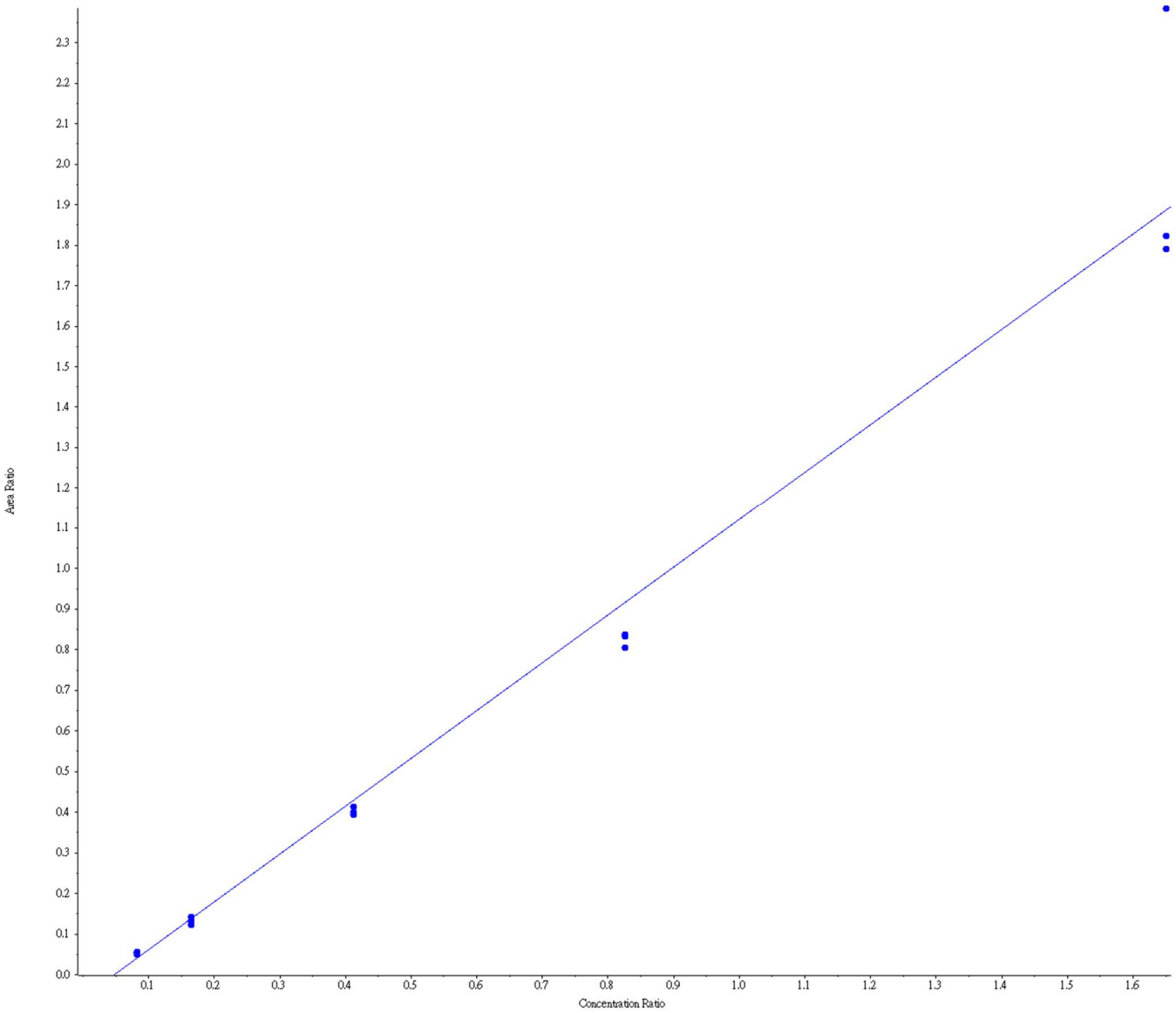
Analyte Name: **SAMP.VGEYSLYIGR.2/y4.M00**

Calibration Equation: y = 0.95859 x + -9.80920e-4 (r = 0.99010) (weighting: 1 / x)



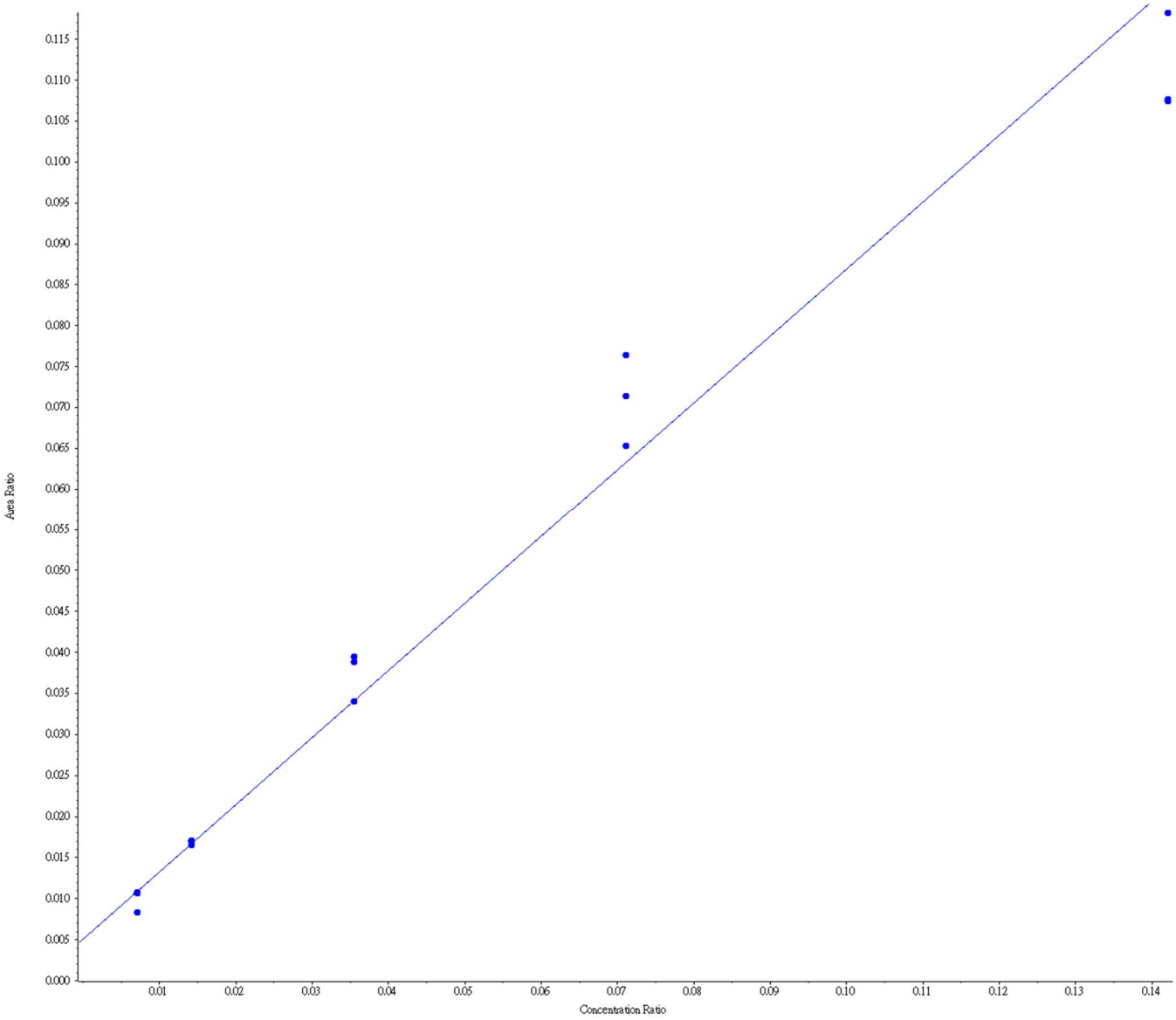
Analyte Name: **ZA2G.EIPAWVPFDPAAQITK.2/y10.M00**

Calibration Equation: y = 1.17735 x + -0.05614 (r = 0.98824) (weighting: 1 / x)



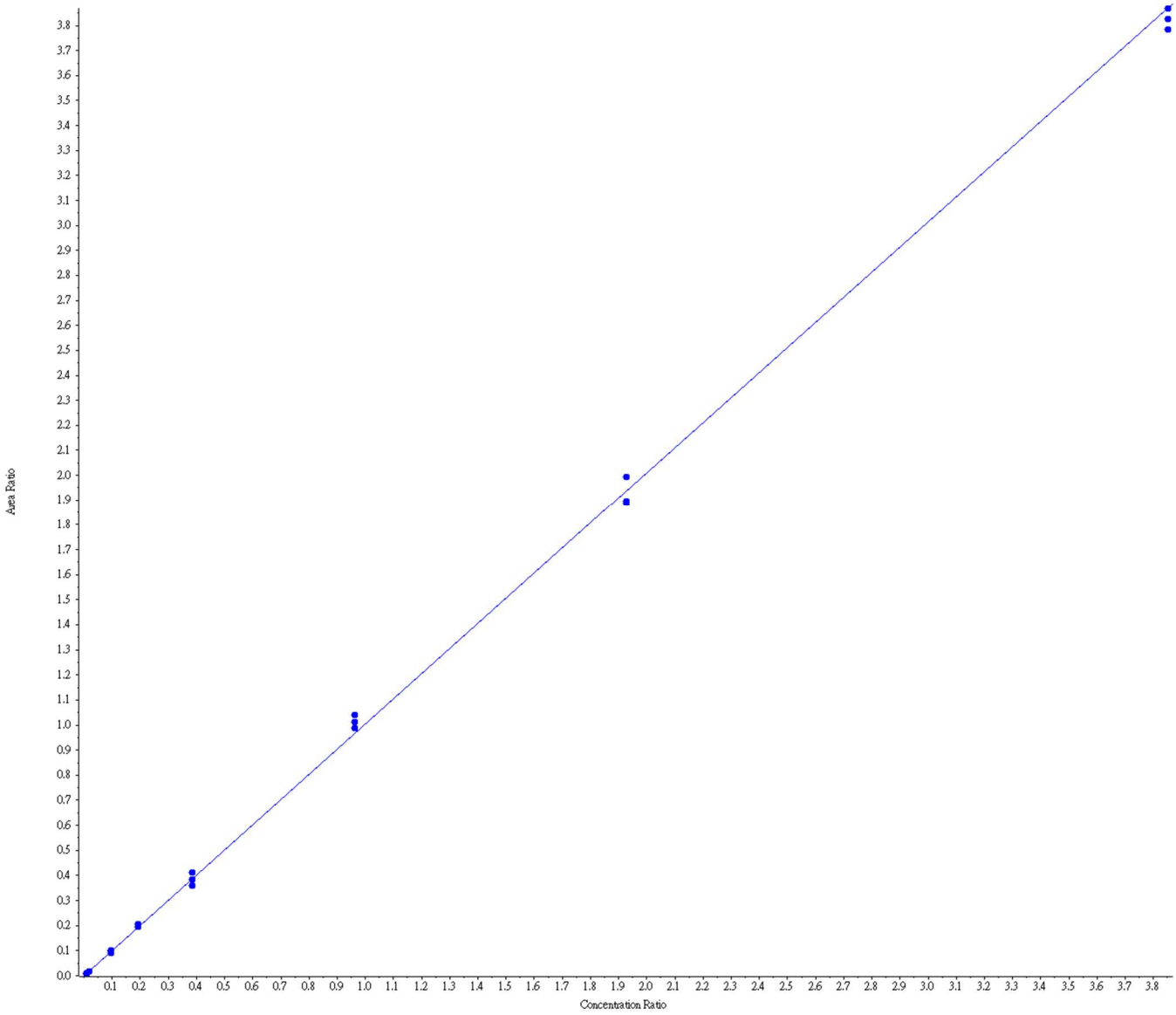
Analyte Name: **FA12.VVGGLVALR.2/y7.M00**

Calibration Equation: y = 0.81853 x + 0.00508 (r = 0.98795) (weighting: 1 / x)



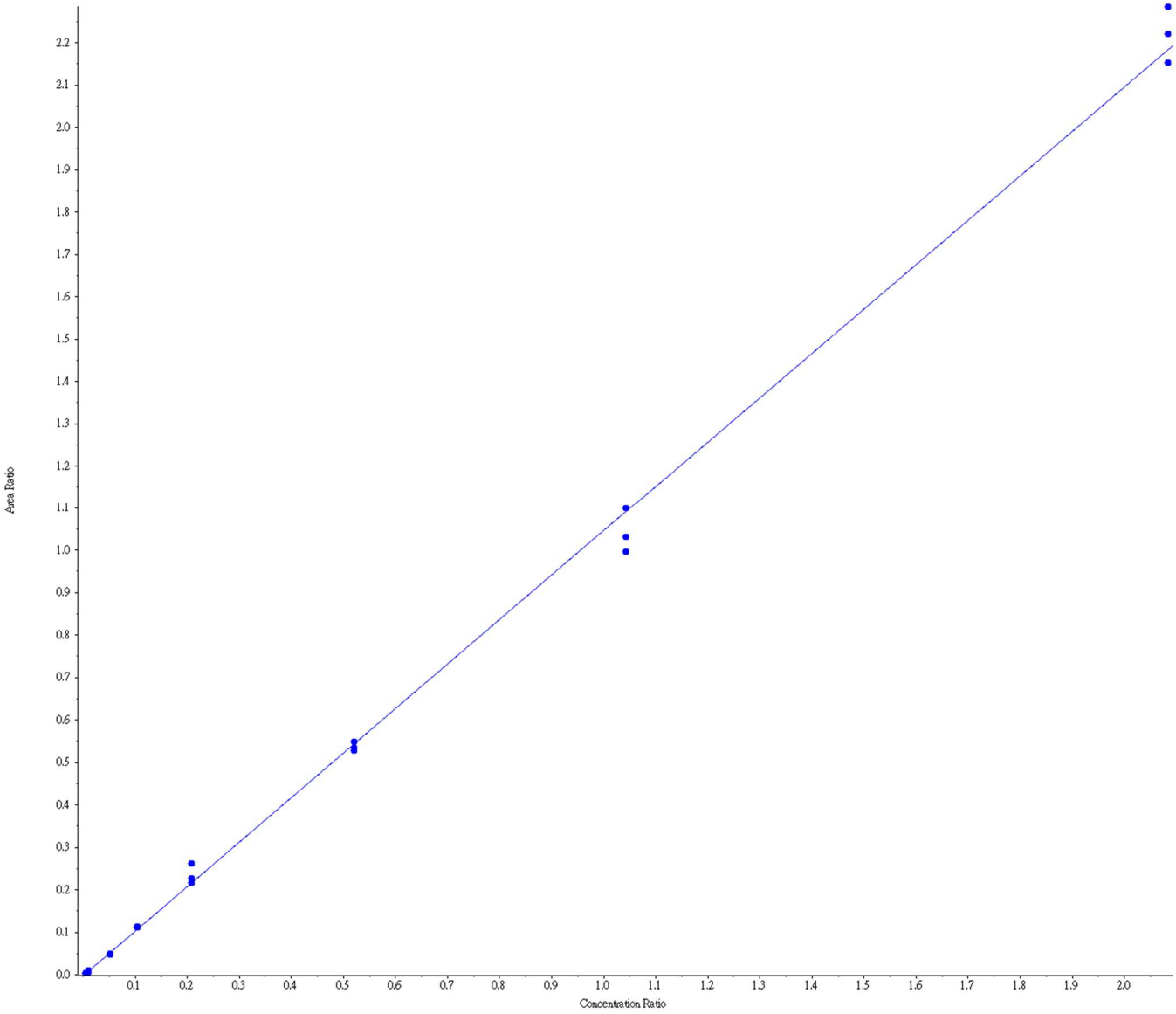
Analyte Name: **CO3.TGLQEVEVK.2/y6.M00**

Calibration Equation: y = 1.00505 x + -4.91033e-4 (r = 0.99951) (weighting: 1 / x)



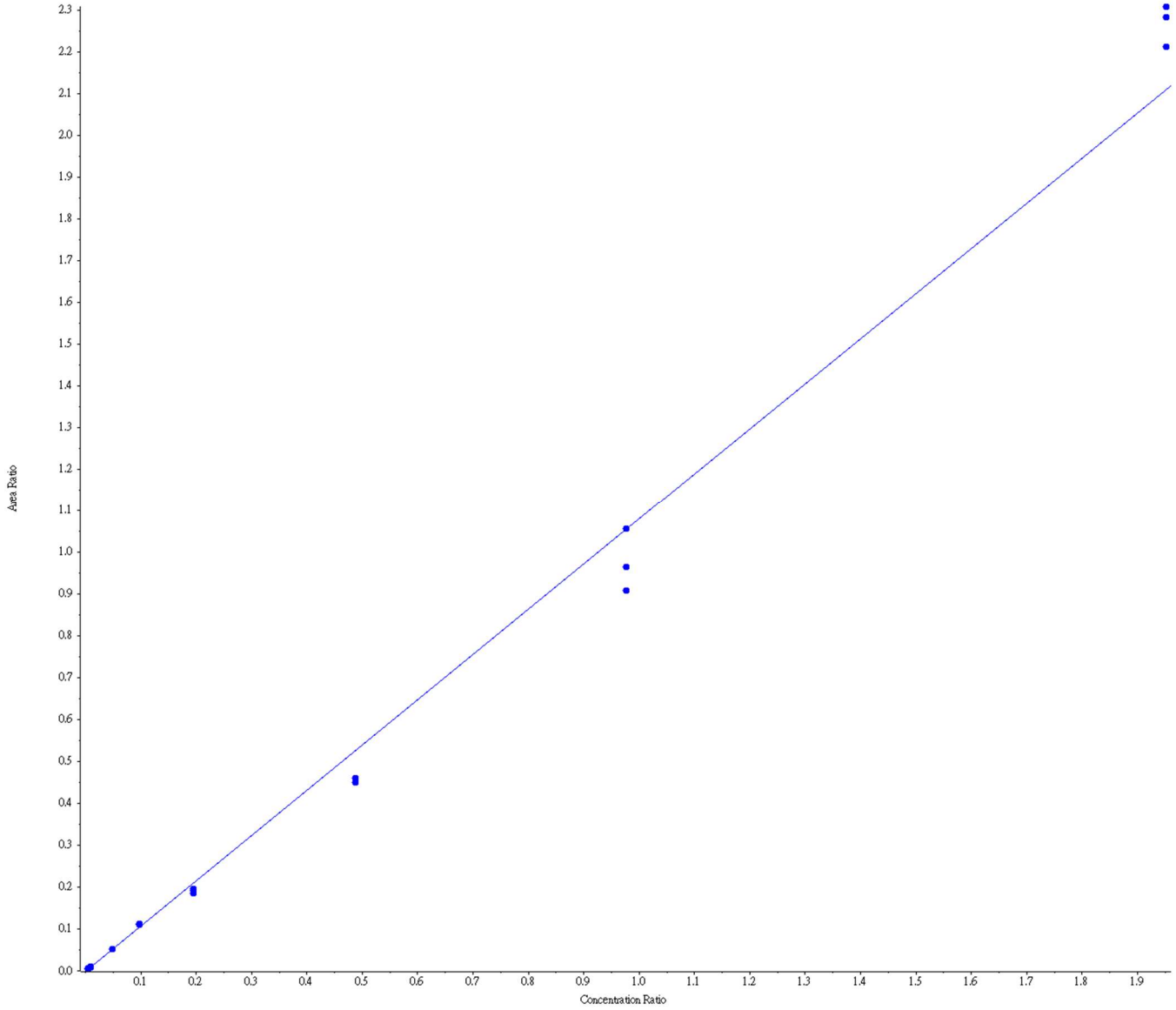
Analyte Name: **FINC.VPGTSTSATLTGLTR.2/y14(2+).M00**

Calibration Equation: y = 1.04893 x + -0.00250 (r = 0.99870) (weighting: 1 / x)



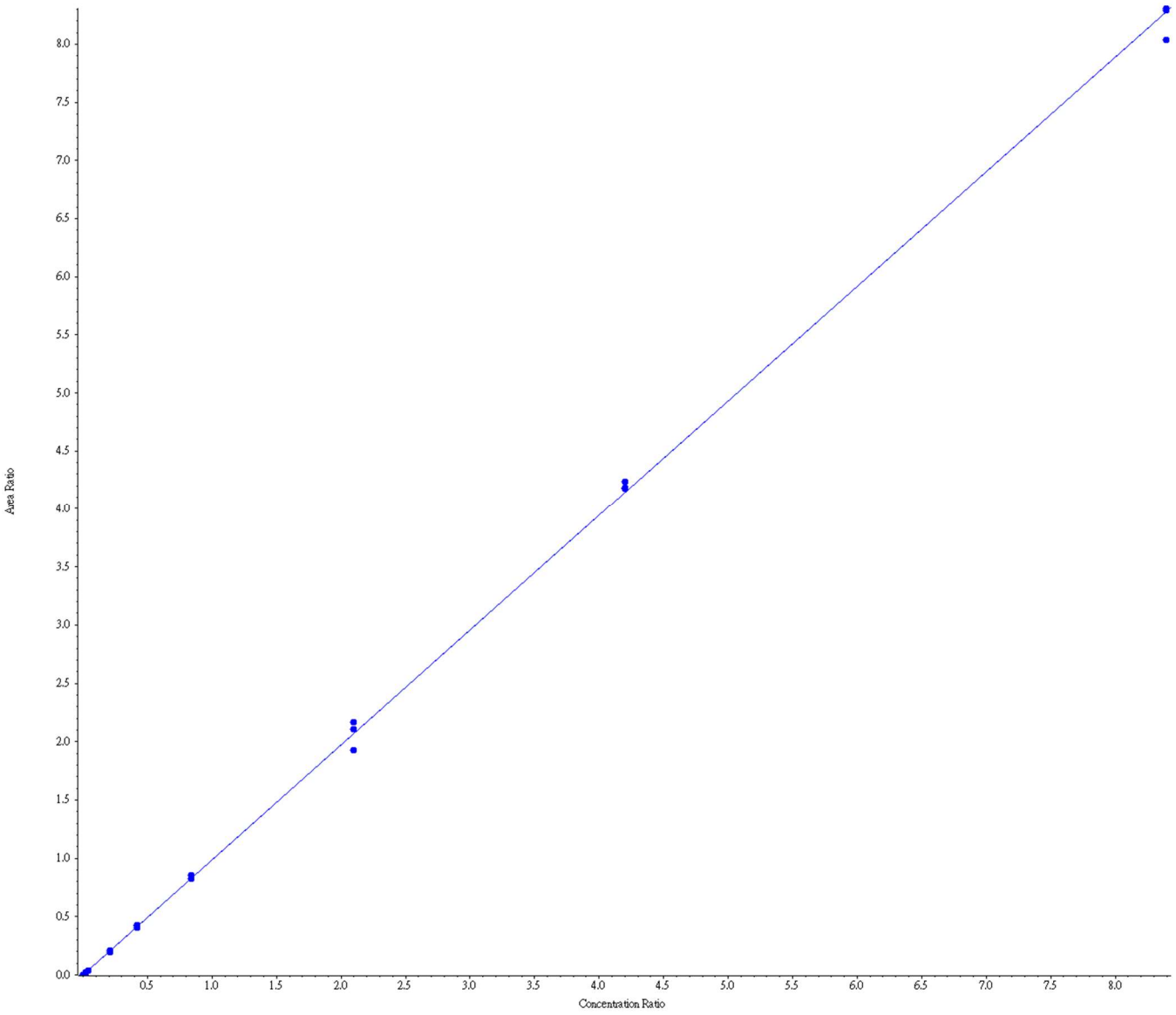
Analyte Name: **HPT.VGYVSGWGR.2/y5.M00**

Calibration Equation: y = 1.08141 x + -0.00123 (r = 0.99570) (weighting: 1 / x)



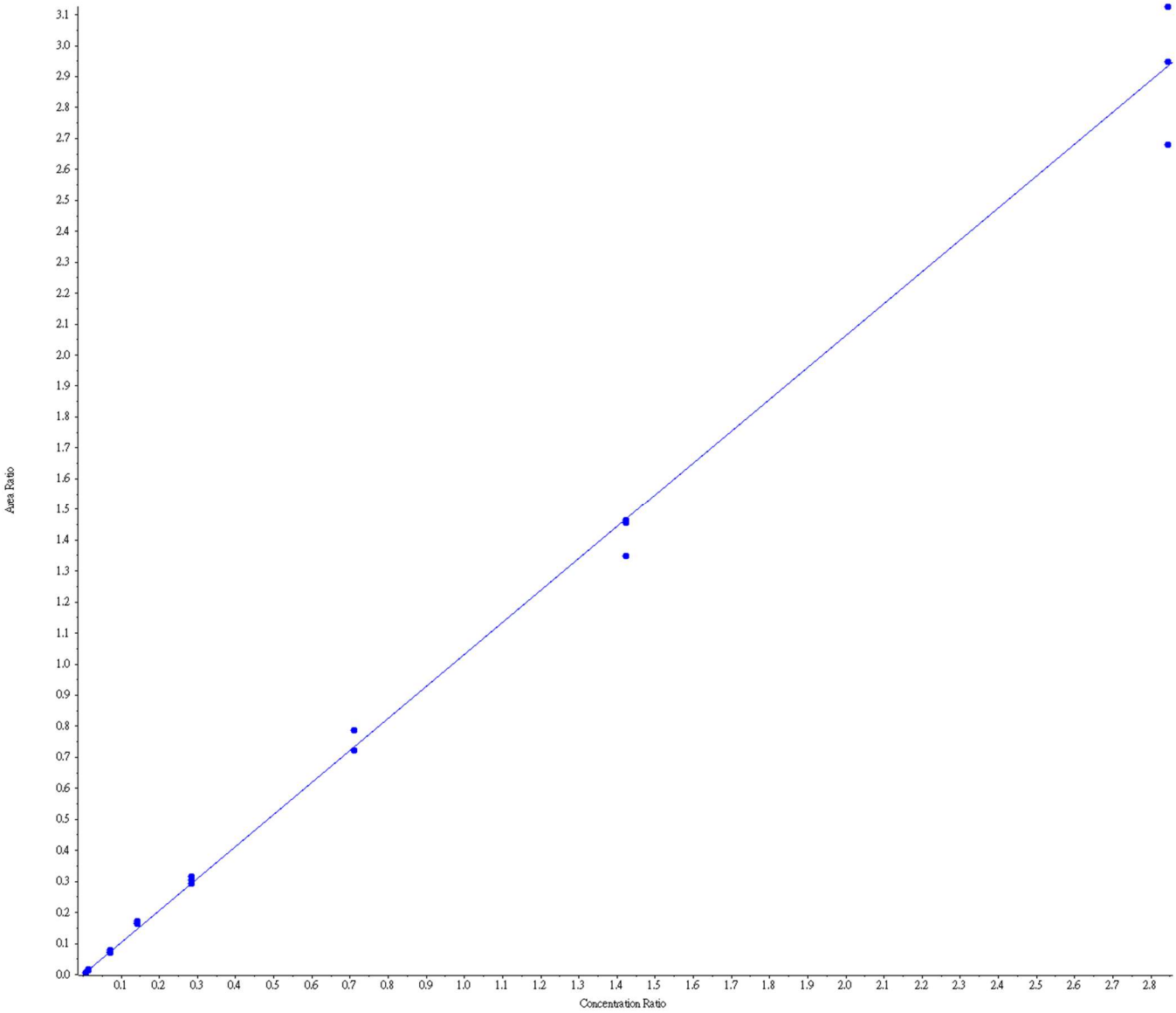
Analyte Name: **HEMO.NFPSPVDAAFR.2/y9(2+).M00**

Calibration Equation: y = 0.98605 x + 2.47303e-4 (r = 0.99968) (weighting: 1 / x)



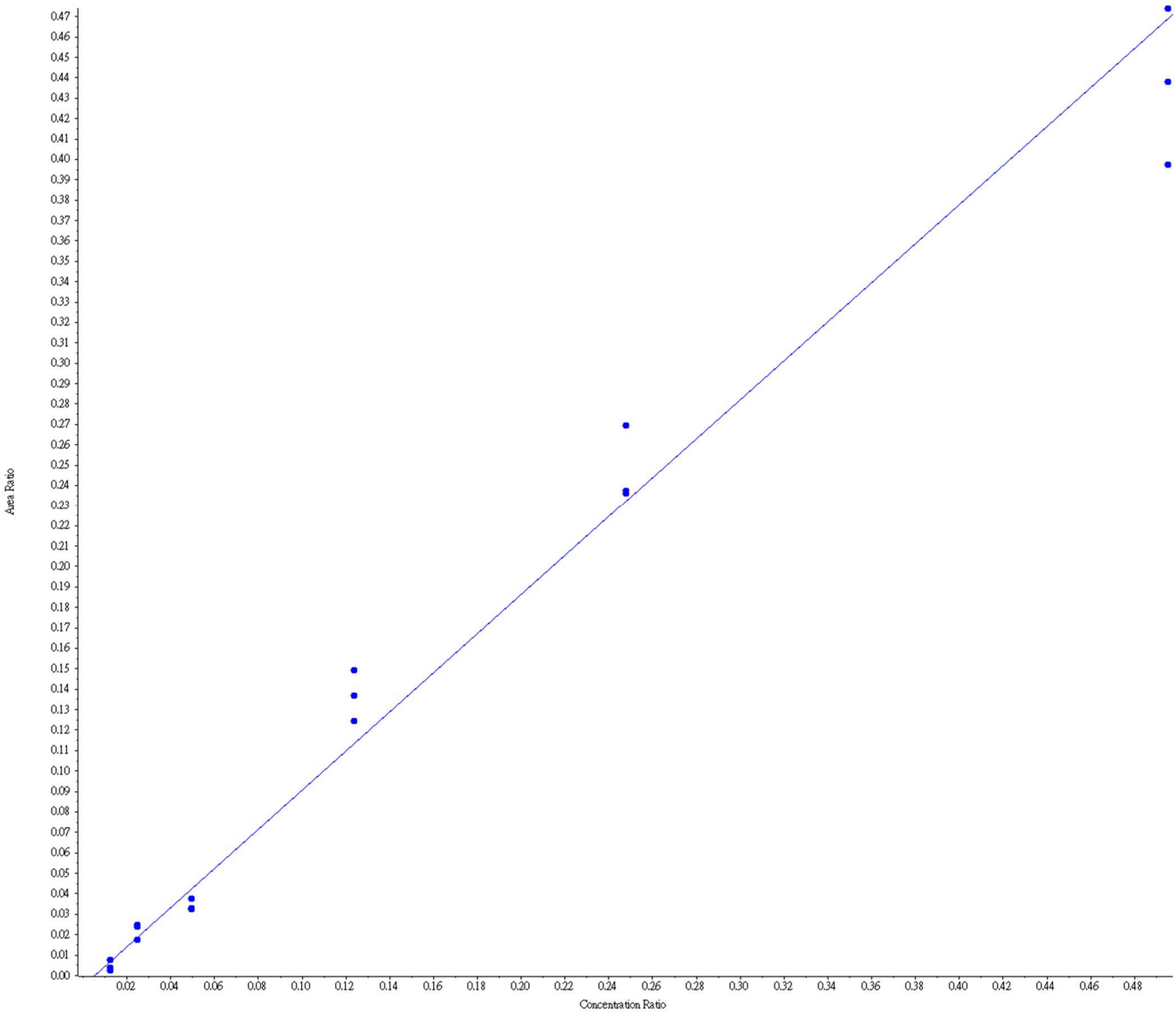
Analyte Name: **HRG.DGYLFQLLR.2/y5.M00**

Calibration Equation: y = 1.03138 x + 4.24995e-4 (r = 0.99803) (weighting: 1 / x)



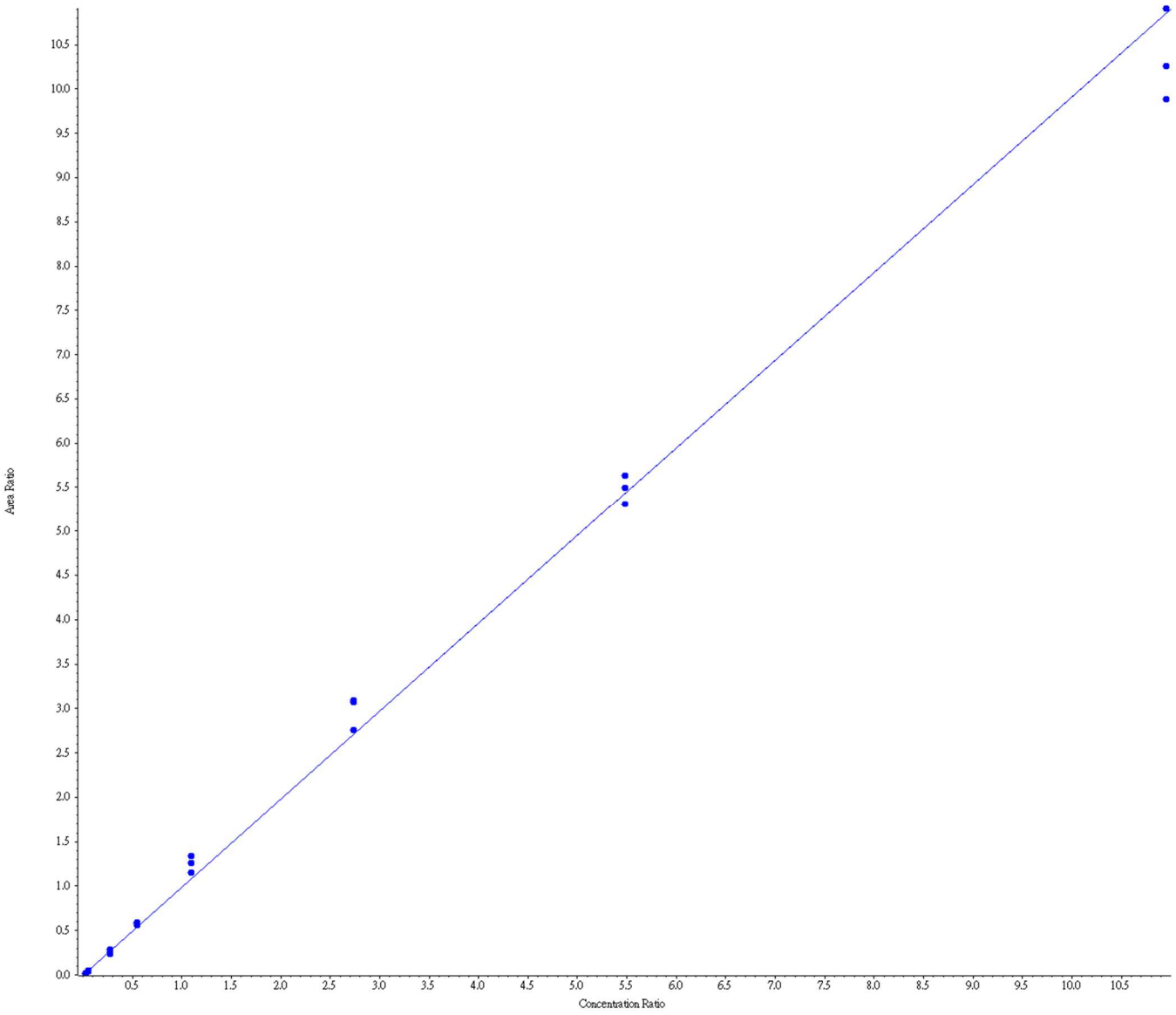
Analyte Name: **Q9UJ43.AEIEYLEK.2/y6.M00**

Calibration Equation: y = 0.95713 x + -0.00503 (r = 0.98935) (weighting: 1 / x)



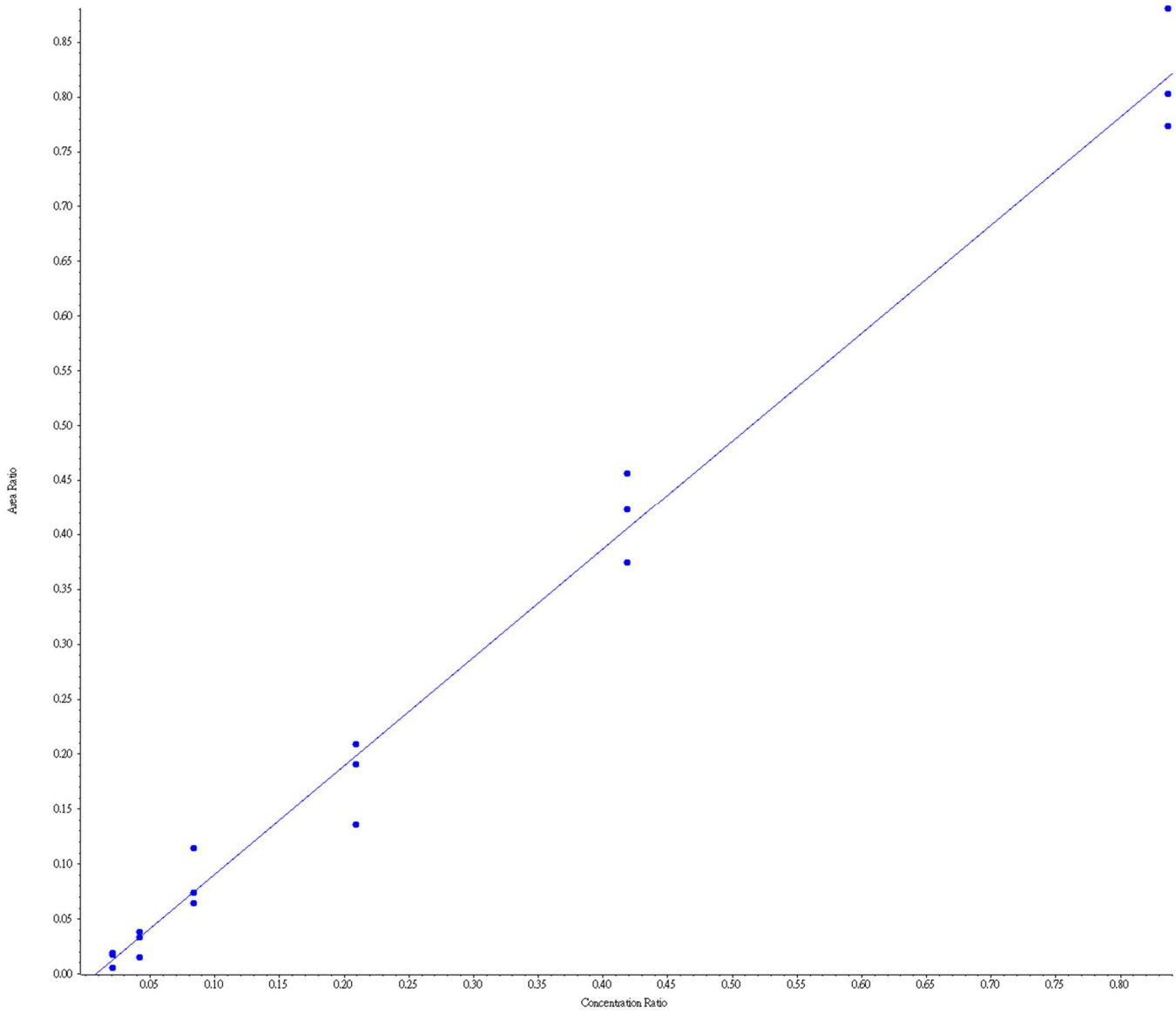
Analyte Name: **VTNC.FEDGVLDPDYPR.2/y7.M00**

Calibration Equation: y = 0.99153 x + -0.00406 (r = 0.99707) (weighting: 1 / x)

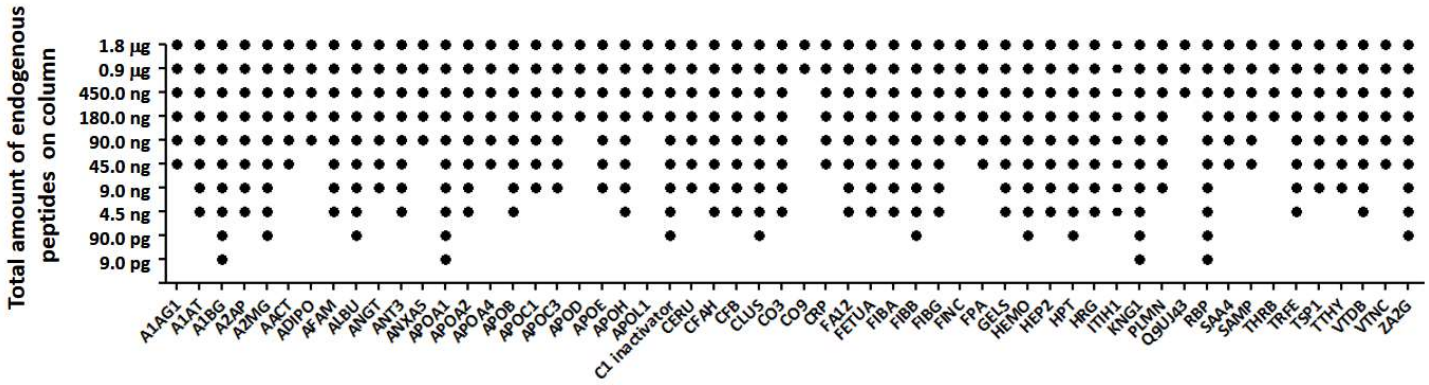


Analyte Name: **FPA.ADSGEGDFLAEGGGVR.2/y7.M00**

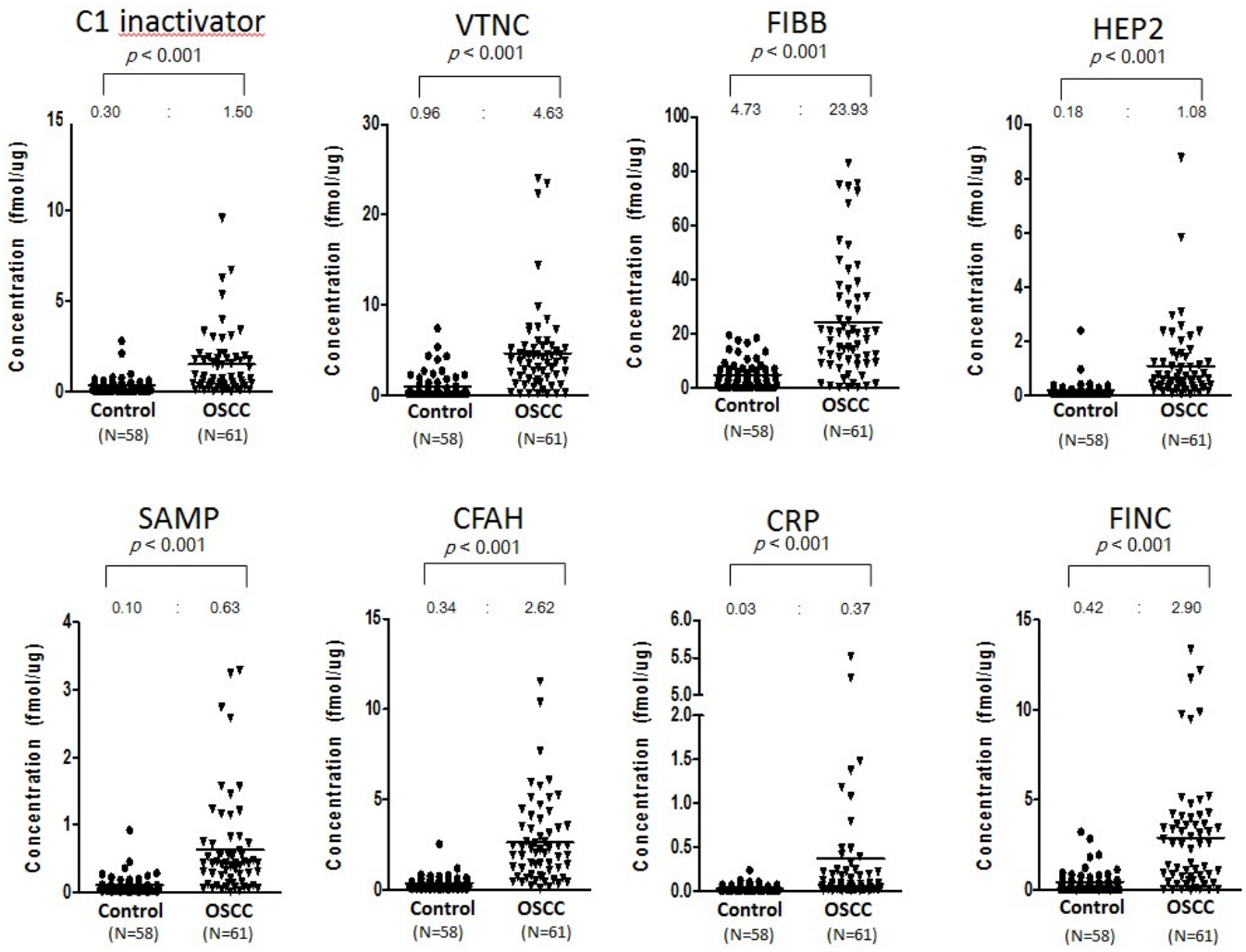
Calibration Equation: y = 0.98725 x + -0.00792 (r = 0.99030) (weighting: 1 / x)

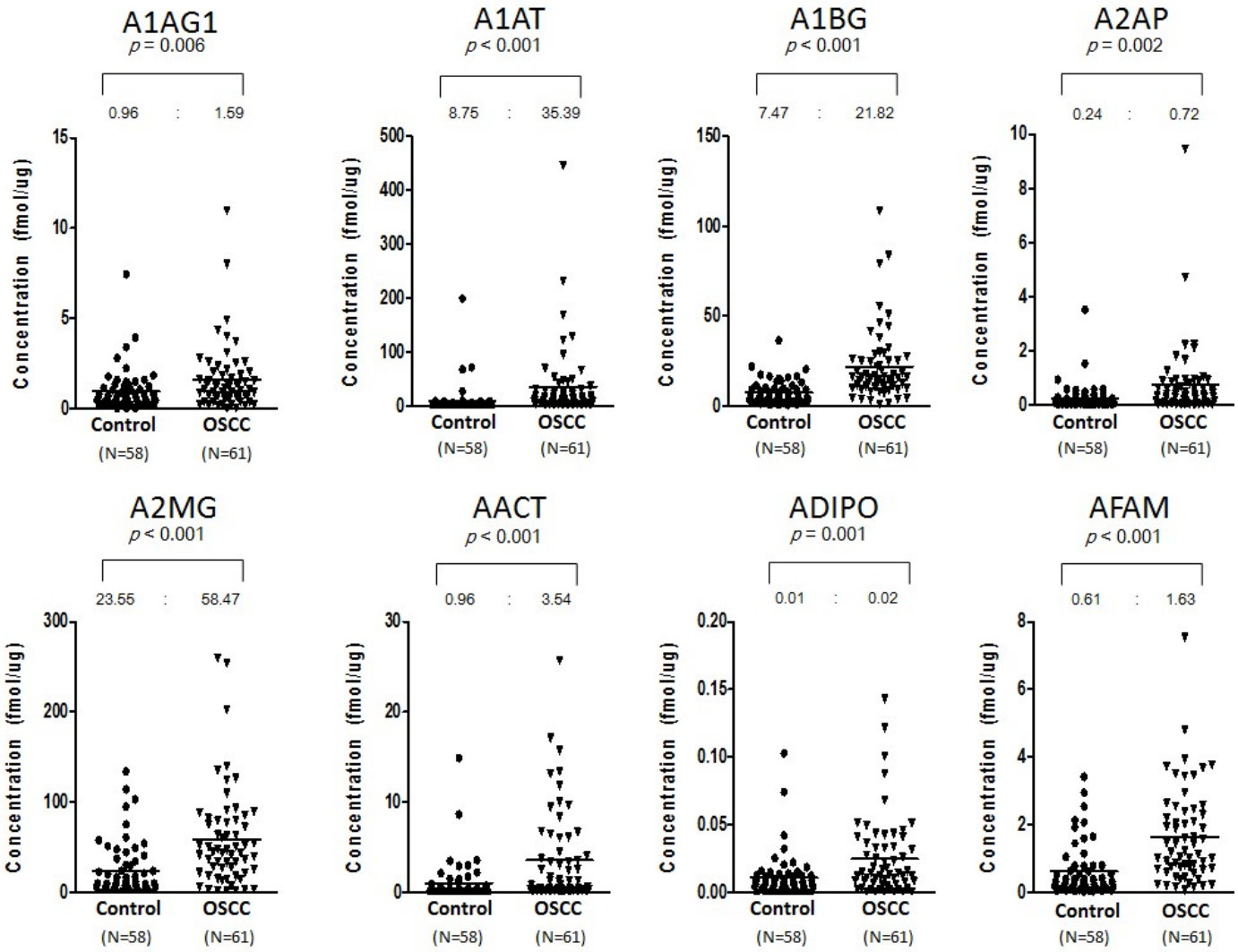


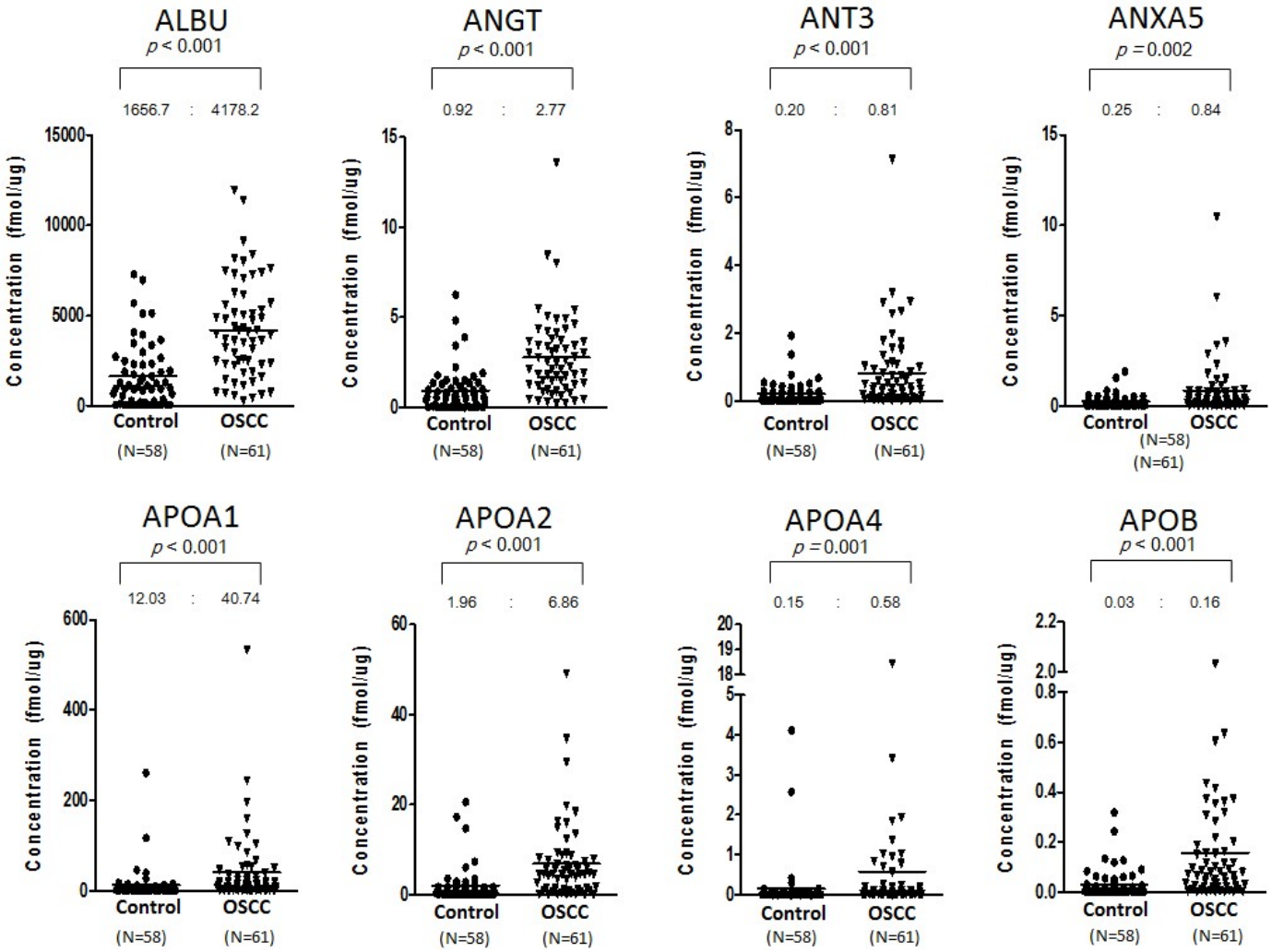
Supplemental Figure S1B. The LLOD and quantifiable concentration points in the standard curves of the 56 targeted endogenous peptide/proteins.

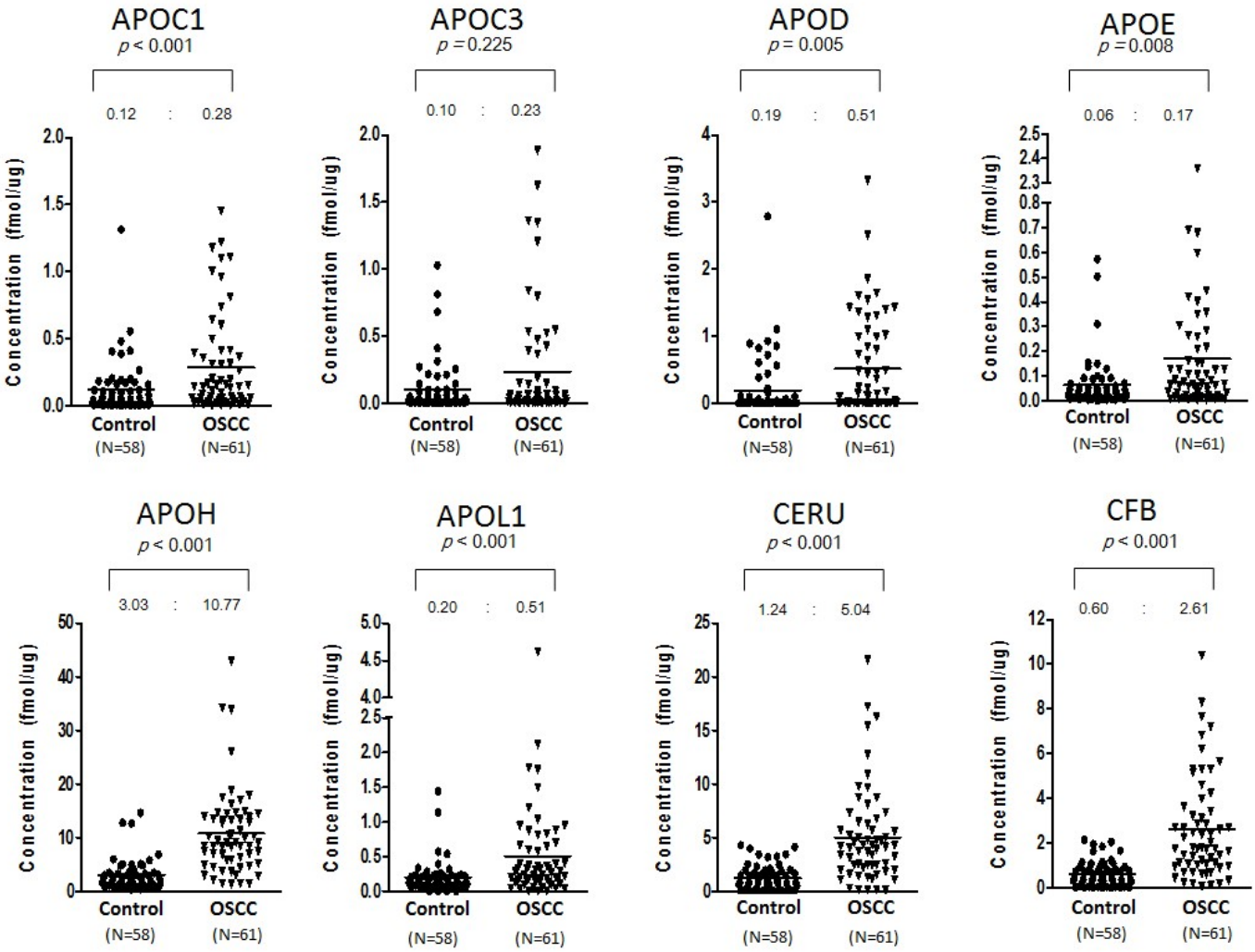


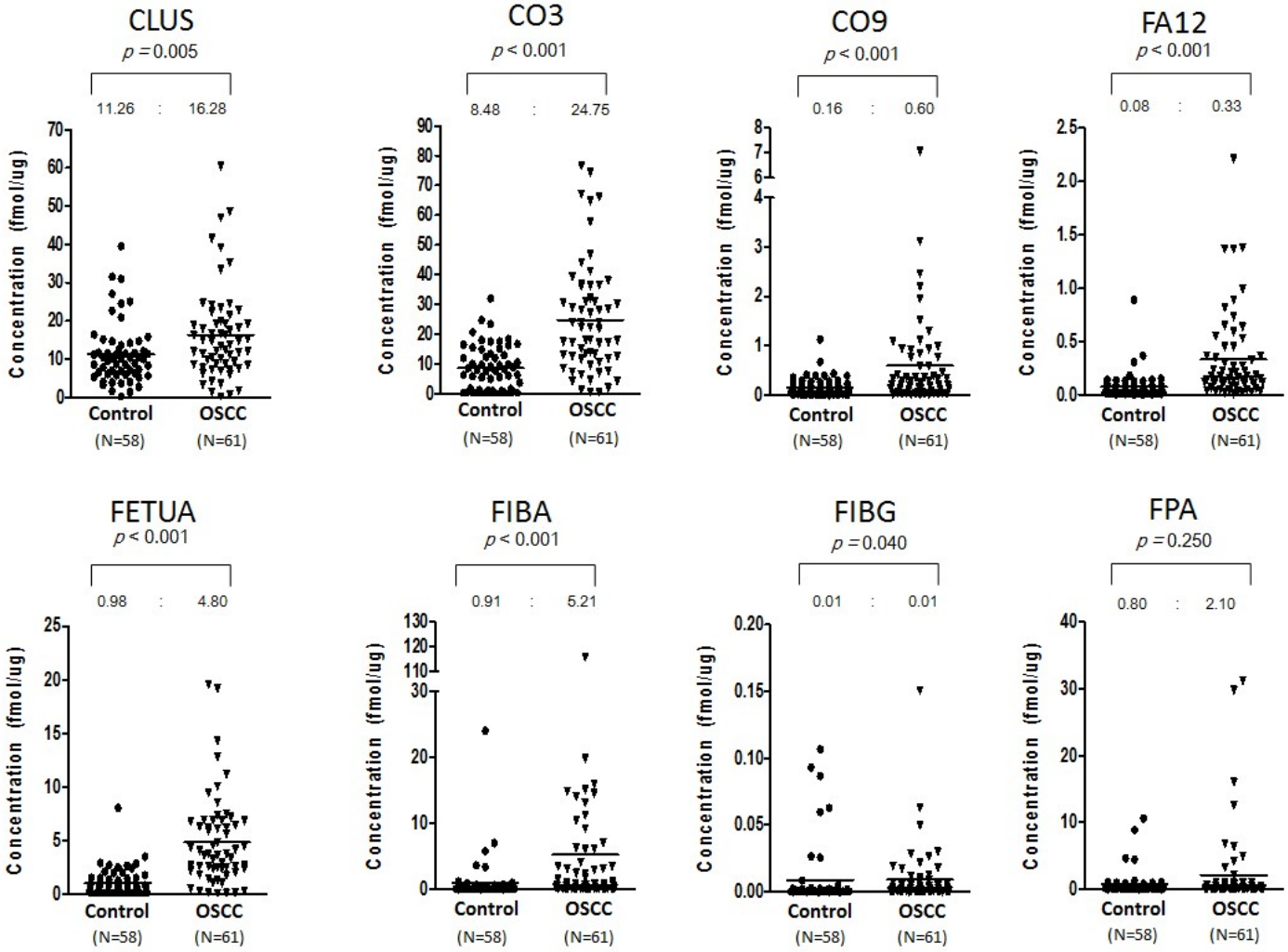
Supplemental Figure S1C Concentration distributions of the 56 proteins in the two clinical states (control and oral cancer), expressed as fmol/μg.

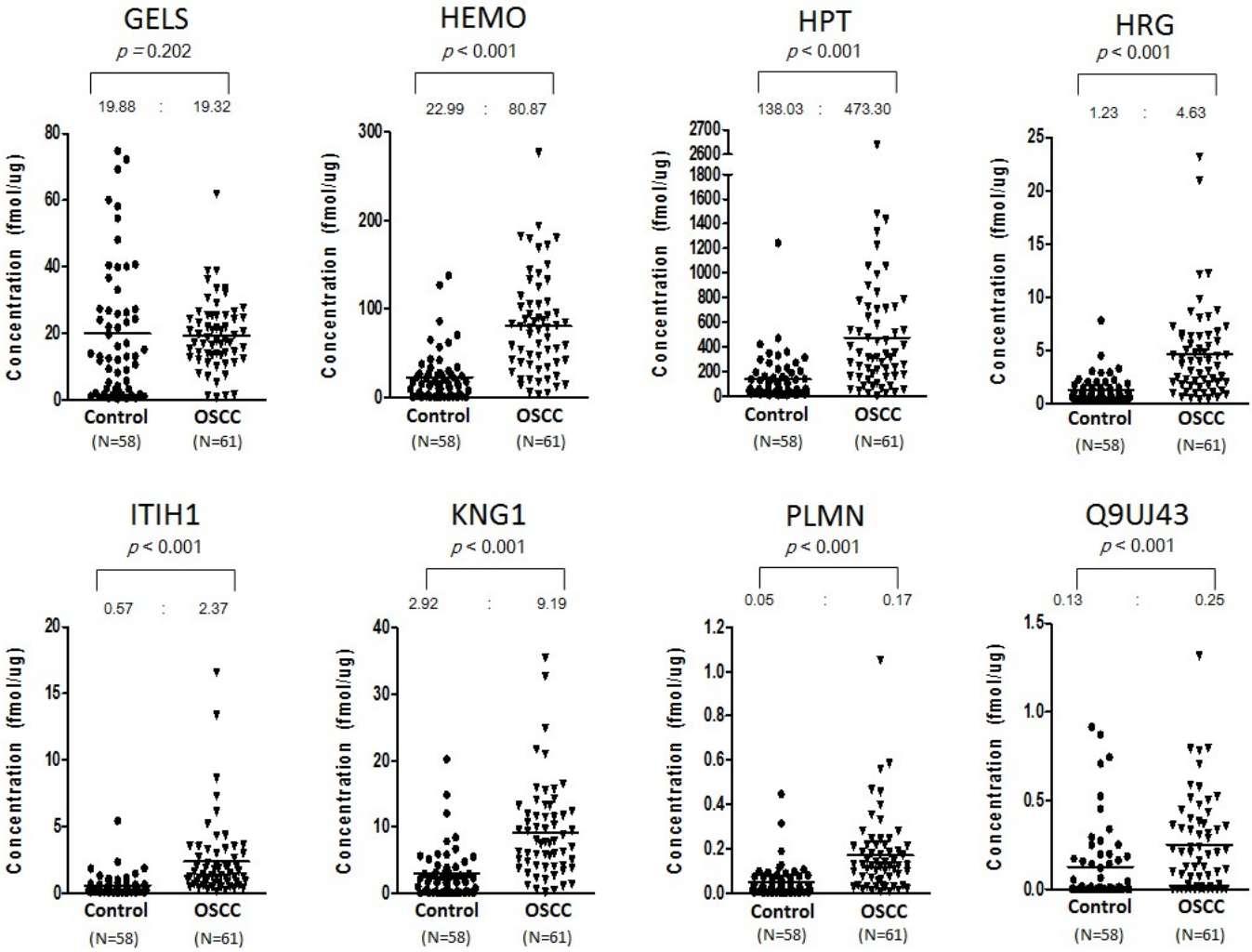


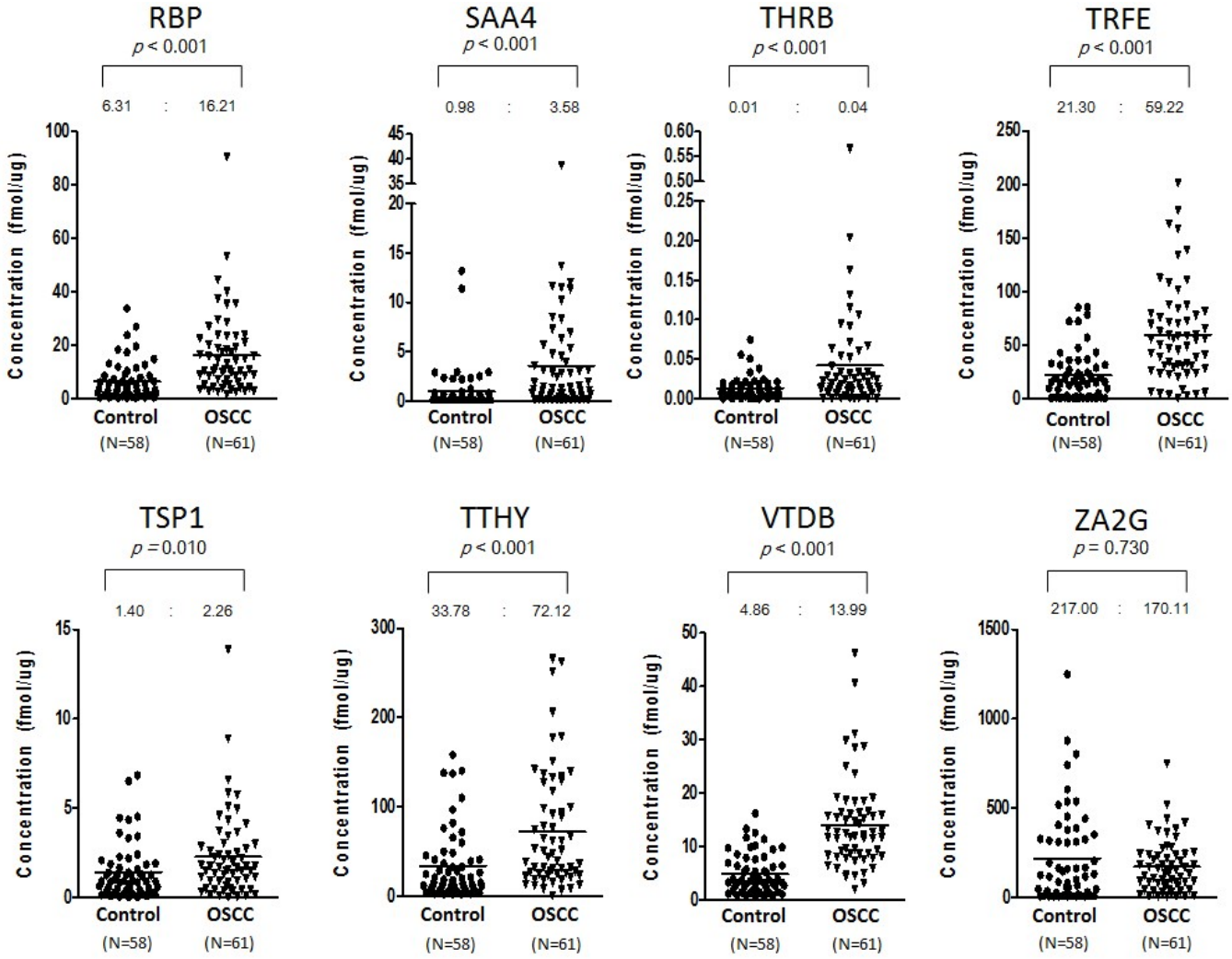

A1AG1
p = 0.006
0.96 : 1.59
A1AT
p < 0.001
8.75 : 35.39
A1BG
p < 0.001
7.47 : 21.82
A2AP
p = 0.002
0.24 : 0.72
A2MG
p < 0.001
23.55 : 58.47
AACT
p < 0.001
0.96 : 3.54
ADIPO
p = 0.001
0.01 : 0.02
AFAM
p < 0.001
0.61 : 1.63
Concentration (fmol/ug)
Control
(N=58)
OSCC
(N=61)


ALBU
p < 0.001
1656.7 : 4178.2
Concentration (fmol/ug)
15000
10000
5000
0
Control
OSCC
(N=58)
(N=61)
ANGT
p < 0.001
0.92 : 2.77
15
10
5
0
ANT3
p < 0.001
0.20 : 0.81
8
6
4
2
0
ANXA5
p = 0.002
0.25 : 0.84
APOA1
p < 0.001
12.03 : 40.74
600
400
200
APOA2
p < 0.001
1.96 : 6.86
60
40
20
APOA4
p = 0.001
0.15 : 0.58
20
19
18
5
4
3
2
1
APOB
p < 0.001
0.03 : 0.16
2.2
2.0
0.8
0.6
0.4
0.2
0.0

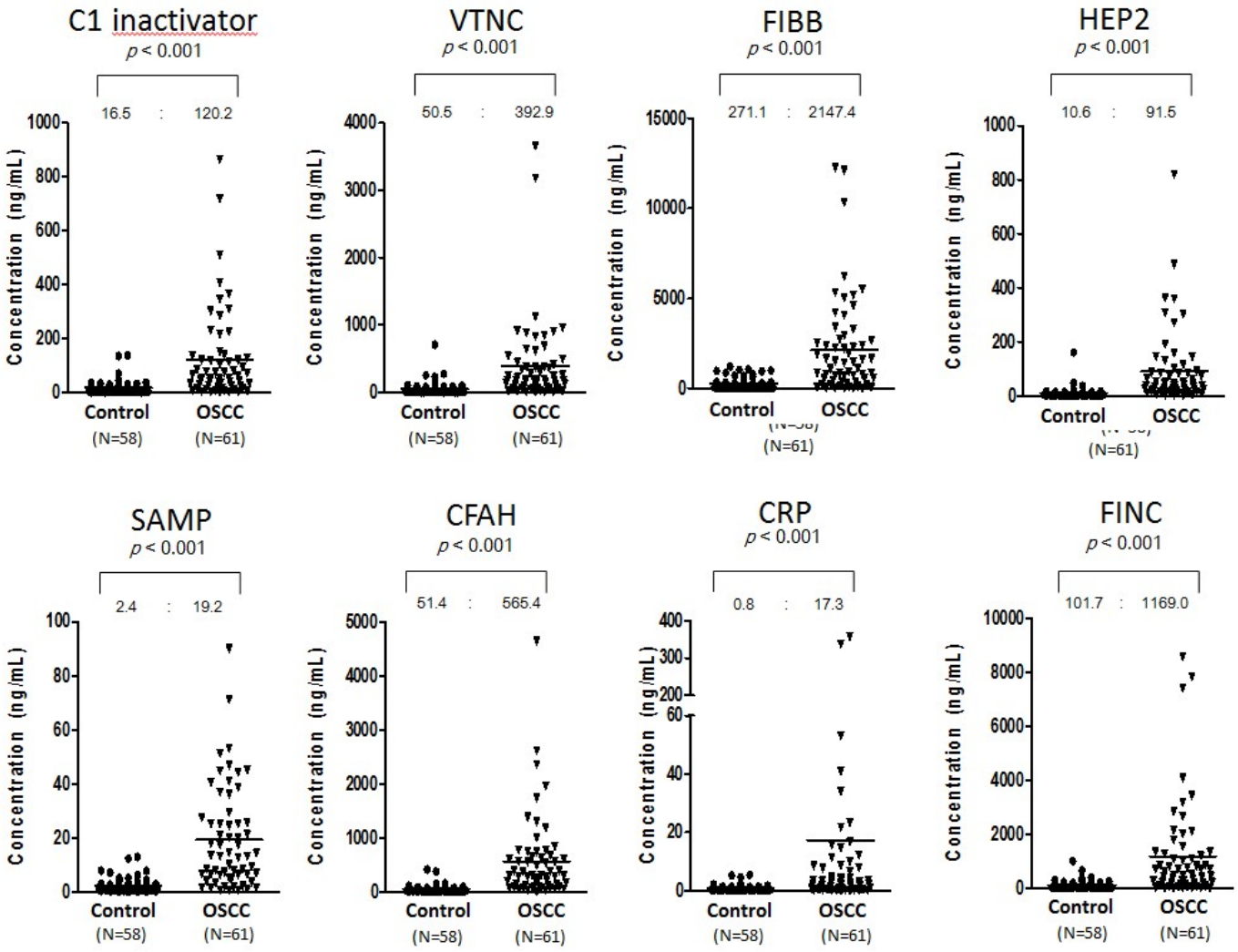

APOC1
p < 0.001
0.12 : 0.28
Concentration (fmol/ug)
Control (N=58)
OSCC (N=61)
APOC3
p = 0.225
0.10 : 0.23
APOD
p = 0.005
0.19 : 0.51
APOE
p = 0.008
0.06 : 0.17
APOH
p < 0.001
3.03 : 10.77
APOL1
p < 0.001
0.20 : 0.51
CERU
p < 0.001
1.24 : 5.04
CFB
p < 0.001
0.60 : 2.61

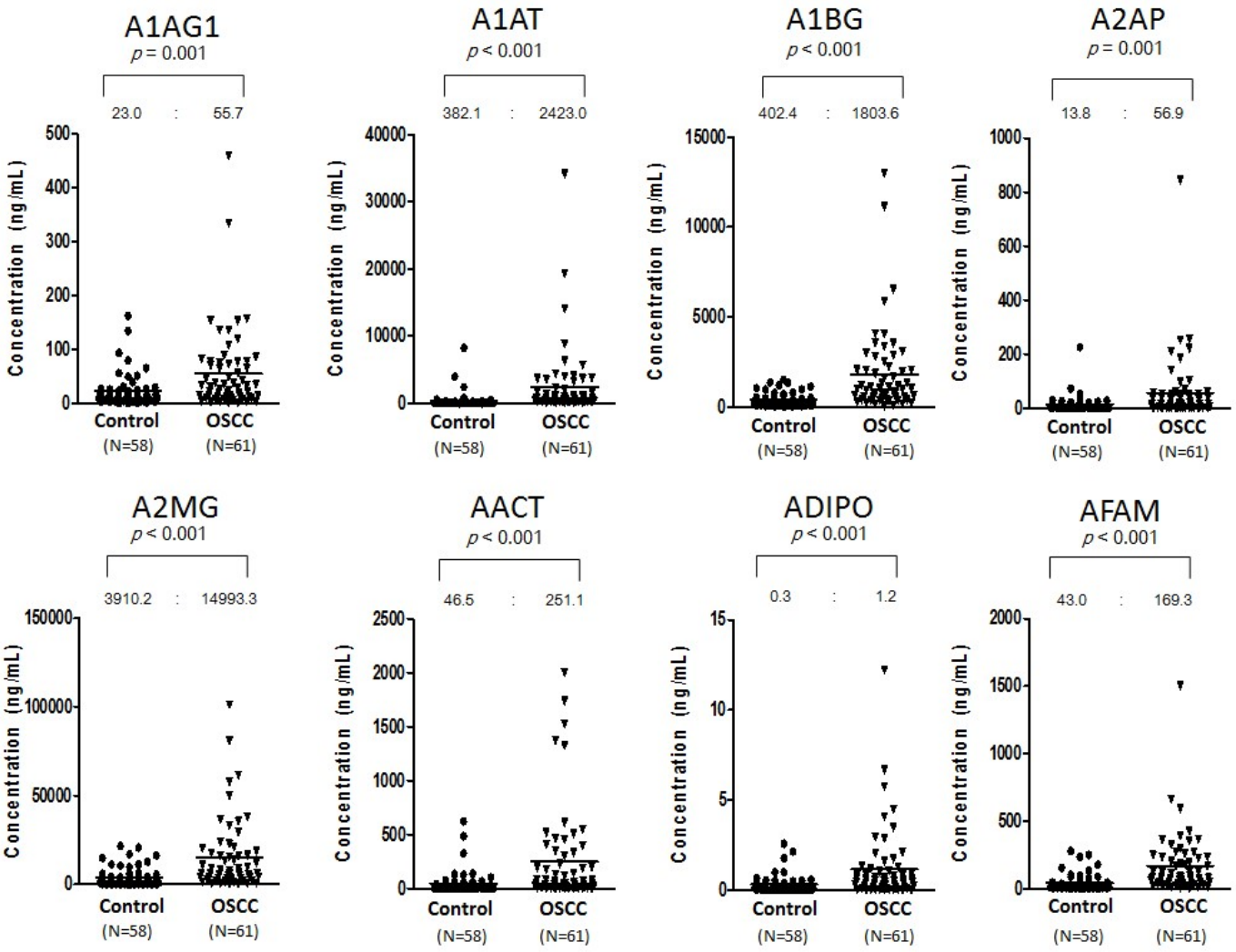

CLUS
p = 0.005
11.26 : 16.28
CO3
p < 0.001
8.48 : 24.75
CO9
p < 0.001
0.16 : 0.60
FA12
p < 0.001
0.08 : 0.33
FETUA
p < 0.001
0.98 : 4.80
FIBA
p < 0.001
0.91 : 5.21
FIBG
p = 0.040
0.01 : 0.01
FPA
p = 0.250
0.80 : 2.10
Concentration (fmol/ug)
Control
(N=58)
OSCC
(N=61)

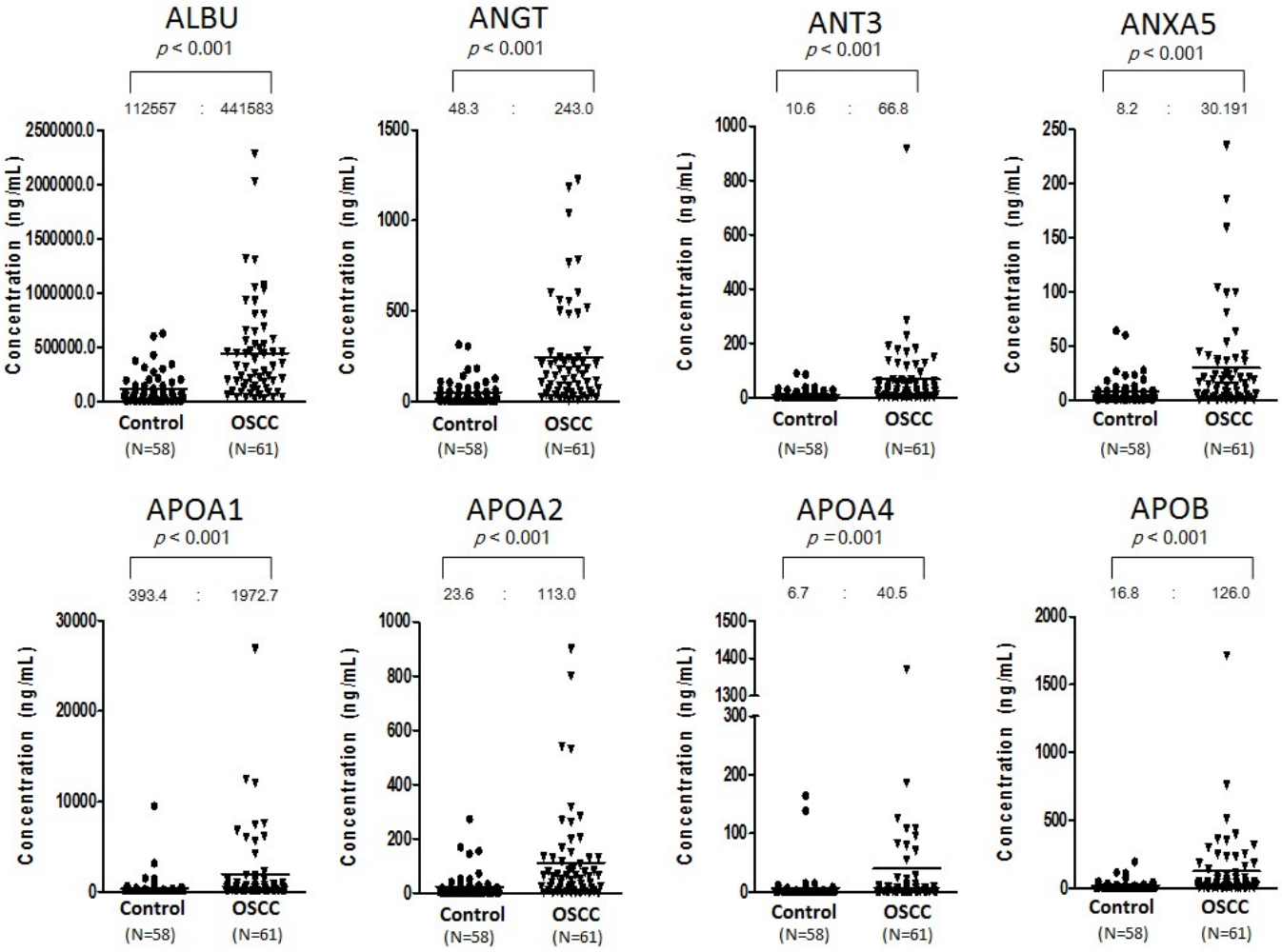

GELS
p = 0.202
19.88 : 19.32
HEMO
p < 0.001
22.99 : 80.87
HPT
p < 0.001
138.03 : 473.30
HRG
p < 0.001
1.23 : 4.63
ITIH1
p < 0.001
0.57 : 2.37
KNG1
p < 0.001
2.92 : 9.19
PLMN
p < 0.001
0.05 : 0.17
Q9UJ43
p < 0.001
0.13 : 0.25
Concentration (fmol/ug)
Control
(N=58)
OSCC
(N=61)

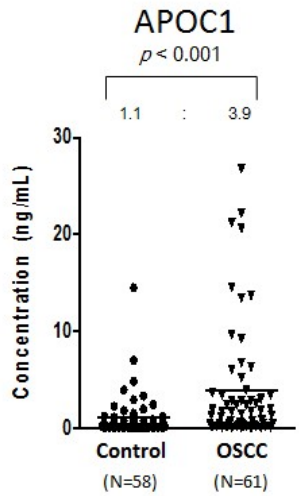

RBP
p < 0.001
6.31 : 16.21
SAA4
p < 0.001
0.98 : 3.58
THRB
p < 0.001
0.01 : 0.04
TRFE
p < 0.001
21.30 : 59.22
TSP1
p = 0.010
1.40 : 2.26
TTHY
p < 0.001
33.78 : 72.12
VTDB
p < 0.001
4.86 : 13.99
ZA2G
p = 0.730
217.00 : 170.11
Concentration (fmol/ug)
Control
(N=58)
OSCC
(N=61)

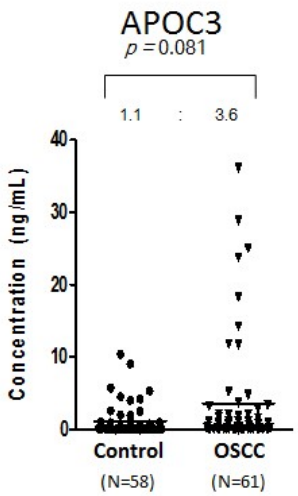
Supplemental Figure S1D Concentration distributions of the 56 proteins in the two clinical states (control and oral cancer), expressed as ng/mL.

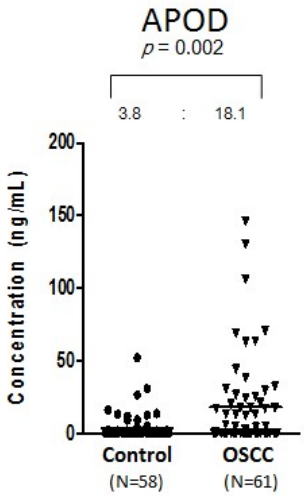


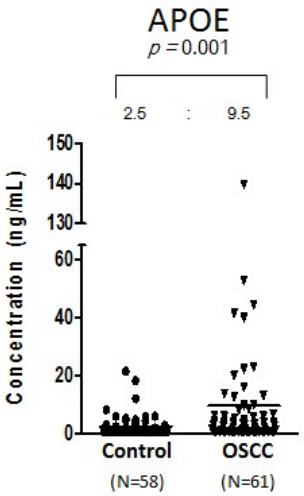

A1AG1
p = 0.001
23.0 : 55.7
Concentration (ng/mL)
Control (N=58)
OSCC (N=61)
A1AT
p < 0.001
382.1 : 2423.0
A1BG
p < 0.001
402.4 : 1803.6
A2AP
p = 0.001
13.8 : 56.9
A2MG
p < 0.001
3910.2 : 14993.3
AACT
p < 0.001
46.5 : 251.1
ADIPO
p < 0.001
0.3 : 1.2
AFAM
p < 0.001
43.0 : 169.3

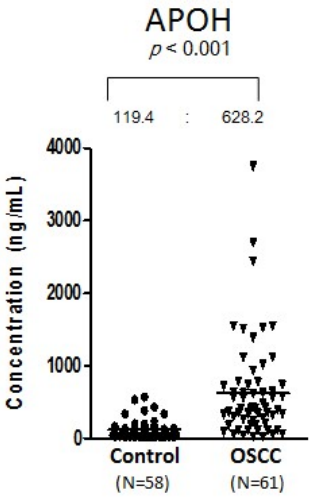

ALBU
p < 0.001
112557 : 441583
Concentration (ng/mL)
2500000.0
2000000.0
1500000.0
1000000.0
500000.0
0.0
Control (N=58)
OSCC (N=61)
ANGT
p < 0.001
48.3 : 243.0
1500
1000
500
0
ANT3
p < 0.001
10.6 : 66.8
1000
800
600
400
200
0
ANXA5
p < 0.001
8.2 : 30.191
250
200
150
100
50
0
APOA1
p < 0.001
393.4 : 1972.7
30000
20000
10000
0
APOA2
p < 0.001
23.6 : 113.0
1000
800
600
400
200
0
APOA4
p = 0.001
6.7 : 40.5
1500
1400
1300
300
200
100
0
APOB
p < 0.001
16.8 : 126.0
2000
1500
1000
500
0

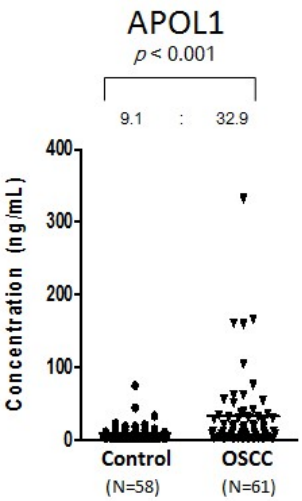

APOC1
p < 0.001
1.1 : 3.9
Concentration (ng/mL)
Control (N=58)
OSCC (N=61)

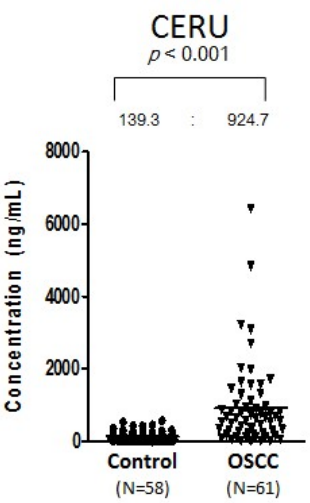

APOC3
p = 0.081
1.1 : 3.6
Concentration (ng/mL)
Control (N=58)
OSCC (N=61)

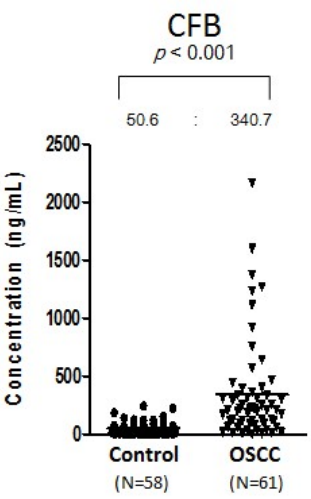

APOD
p = 0.002
3.8 : 18.1
Concentration (ng/mL)
Control (N=58)
OSCC (N=61)

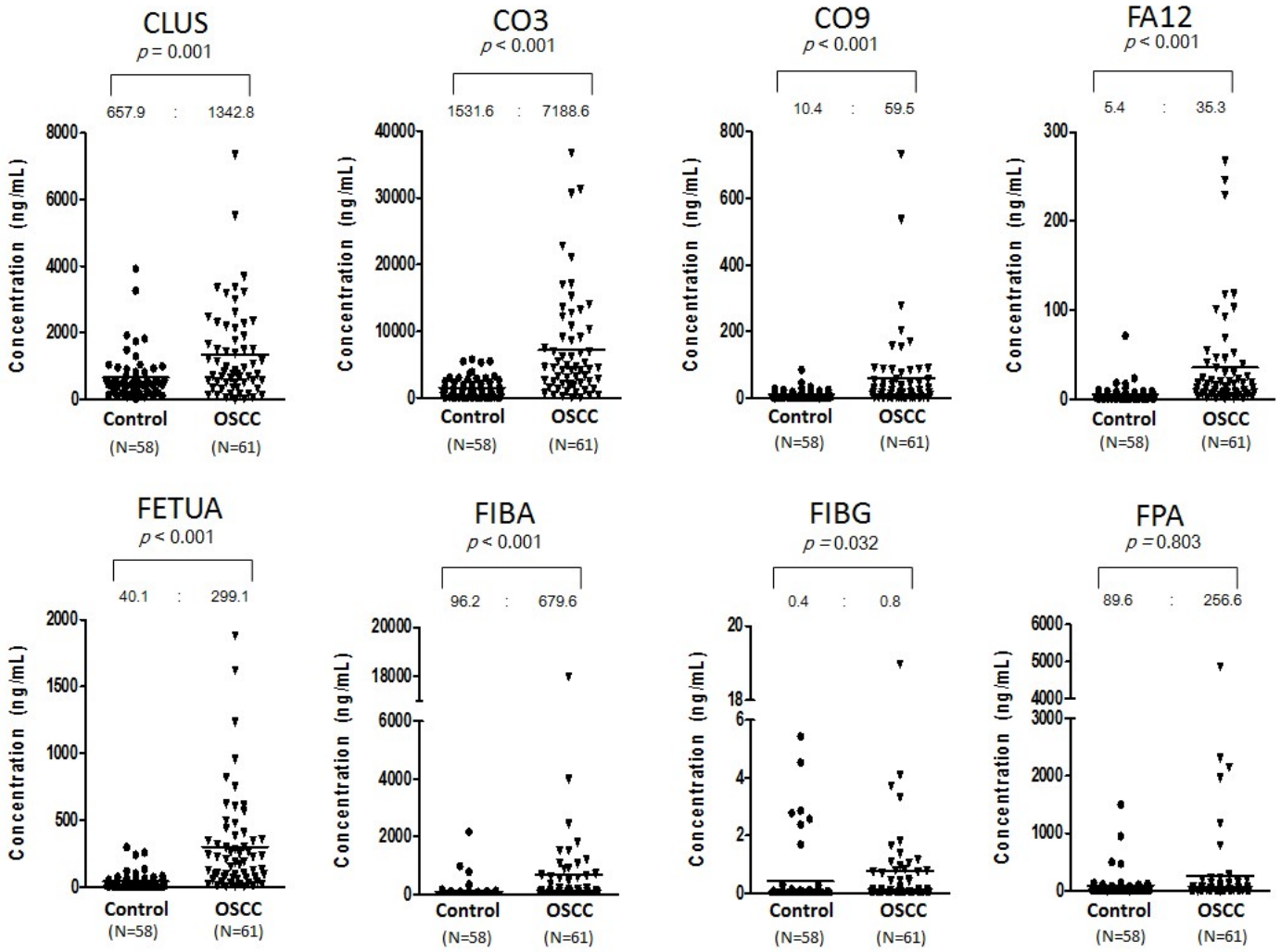

APOE
p = 0.001
2.5 : 9.5
Concentration (ng/mL)
Control (N=58)
OSCC (N=61)

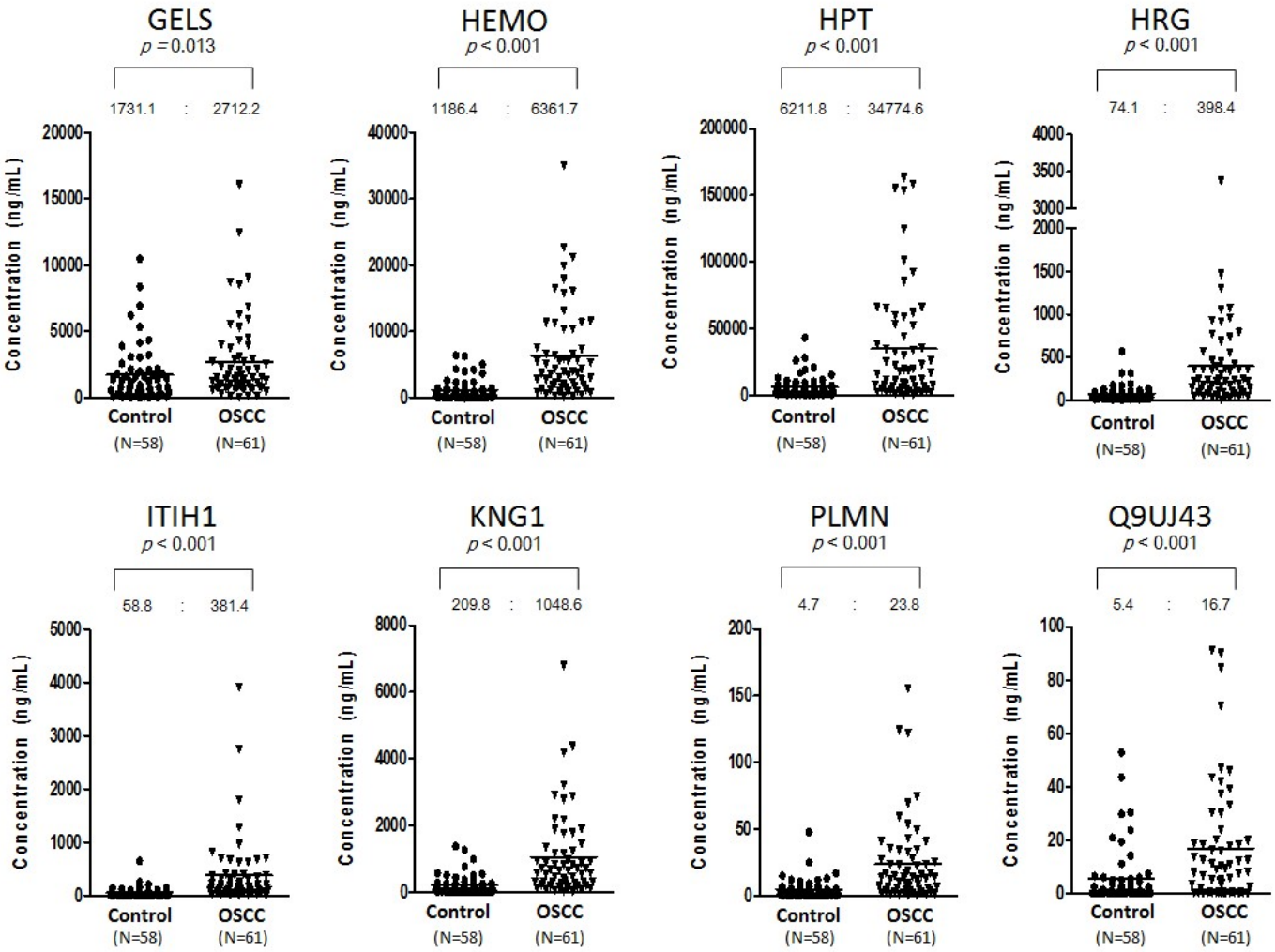

APOH
p < 0.001
119.4 : 628.2
Concentration (ng/mL)
Control (N=58)
OSCC (N=61)

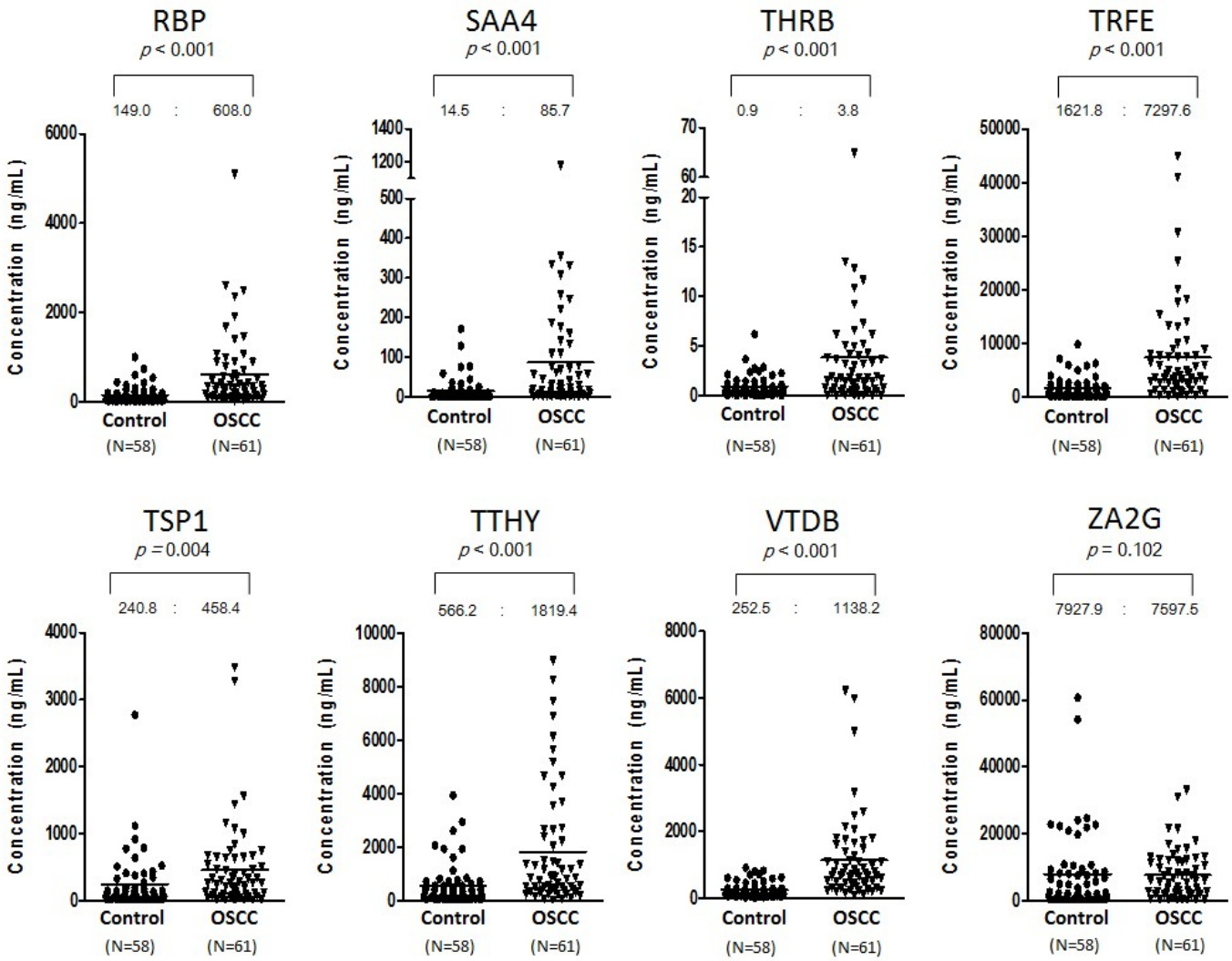

APOL1
p < 0.001
9.1 : 32.9
Concentration (ng/mL)
Control (N=58)
OSCC (N=61)


CERU
p < 0.001
139.3 : 924.7
Concentration (ng/mL)
Control (N=58)
OSCC (N=61)

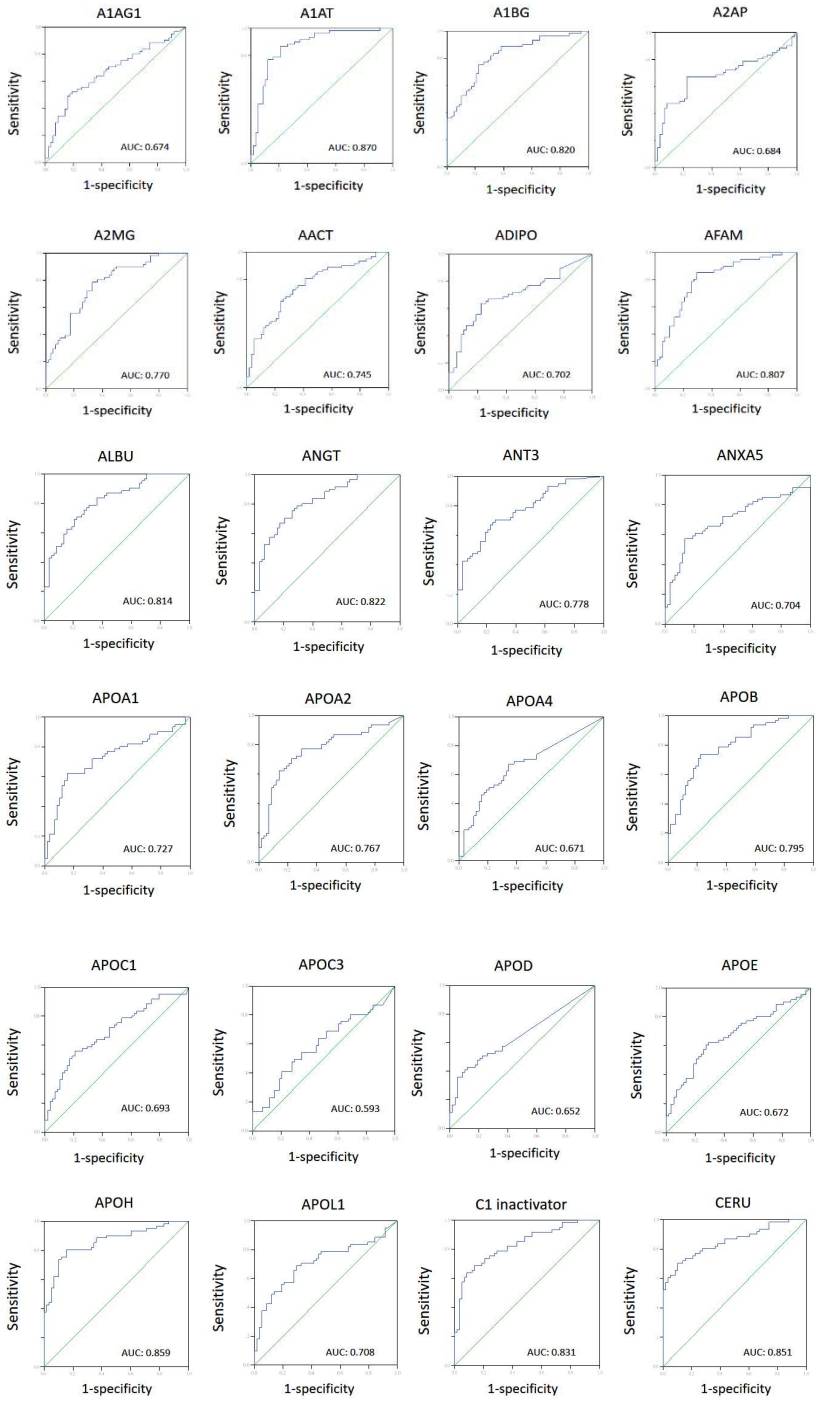

CFB
p < 0.001
50.6 : 340.7
Concentration (ng/mL)
Control (N=58)
OSCC (N=61)

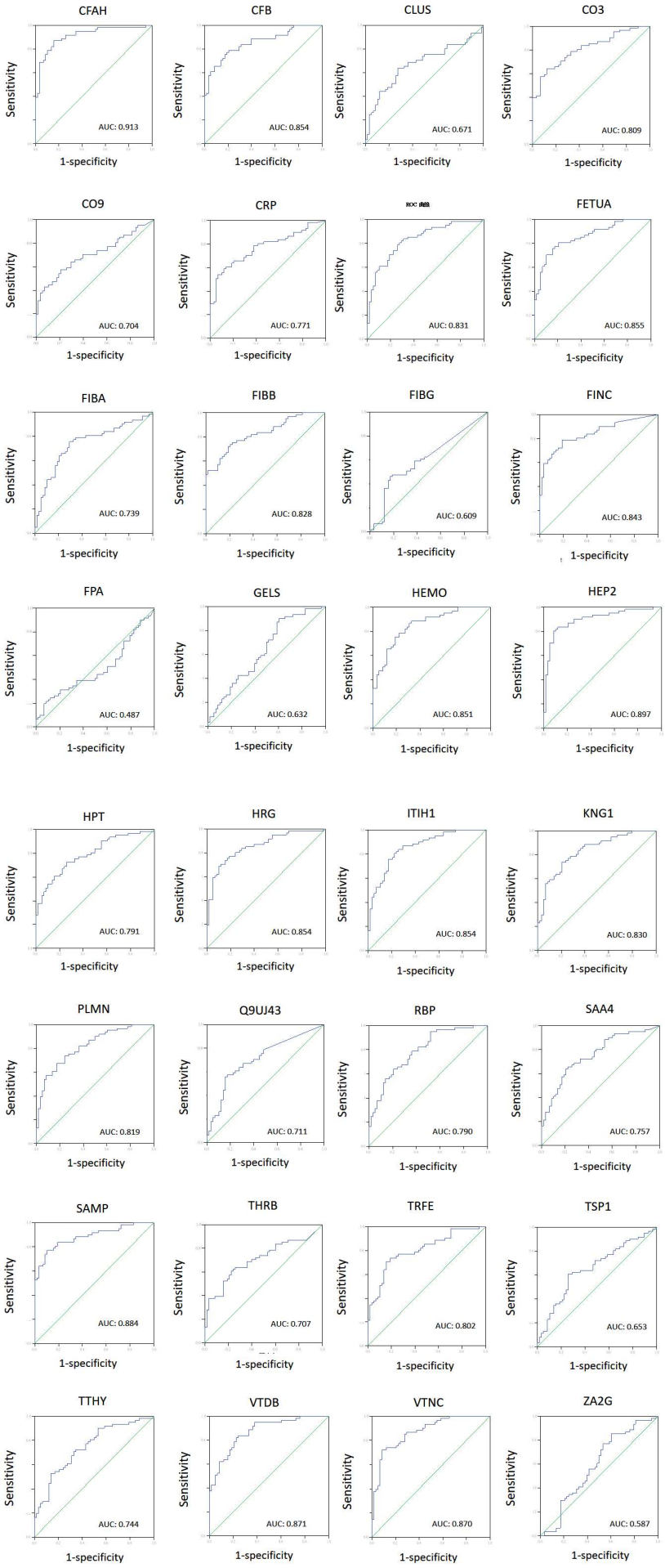

CLUS
p = 0.001
657.9 : 1342.8
Concentration (ng/mL)
Control (N=58)
OSCC (N=61)
CO3
p < 0.001
1531.6 : 7188.6
CO9
p < 0.001
10.4 : 59.5
FA12
p < 0.001
5.4 : 35.3
FETUA
p < 0.001
40.1 : 299.1
FIBA
p < 0.001
96.2 : 679.6
FIBG
p = 0.032
0.4 : 0.8
FPA
p = 0.803
89.6 : 256.6


GELS
p = 0.013
1731.1 : 2712.2
Concentration (ng/mL)
Control (N=58)
OSCC (N=61)
HEMO
p < 0.001
1186.4 : 6361.7
HPT
p < 0.001
6211.8 : 34774.6
HRG
p < 0.001
74.1 : 398.4
ITIH1
p < 0.001
58.8 : 381.4
KNG1
p < 0.001
209.8 : 1048.6
PLMN
p < 0.001
4.7 : 23.8
Q9UJ43
p < 0.001
5.4 : 16.7

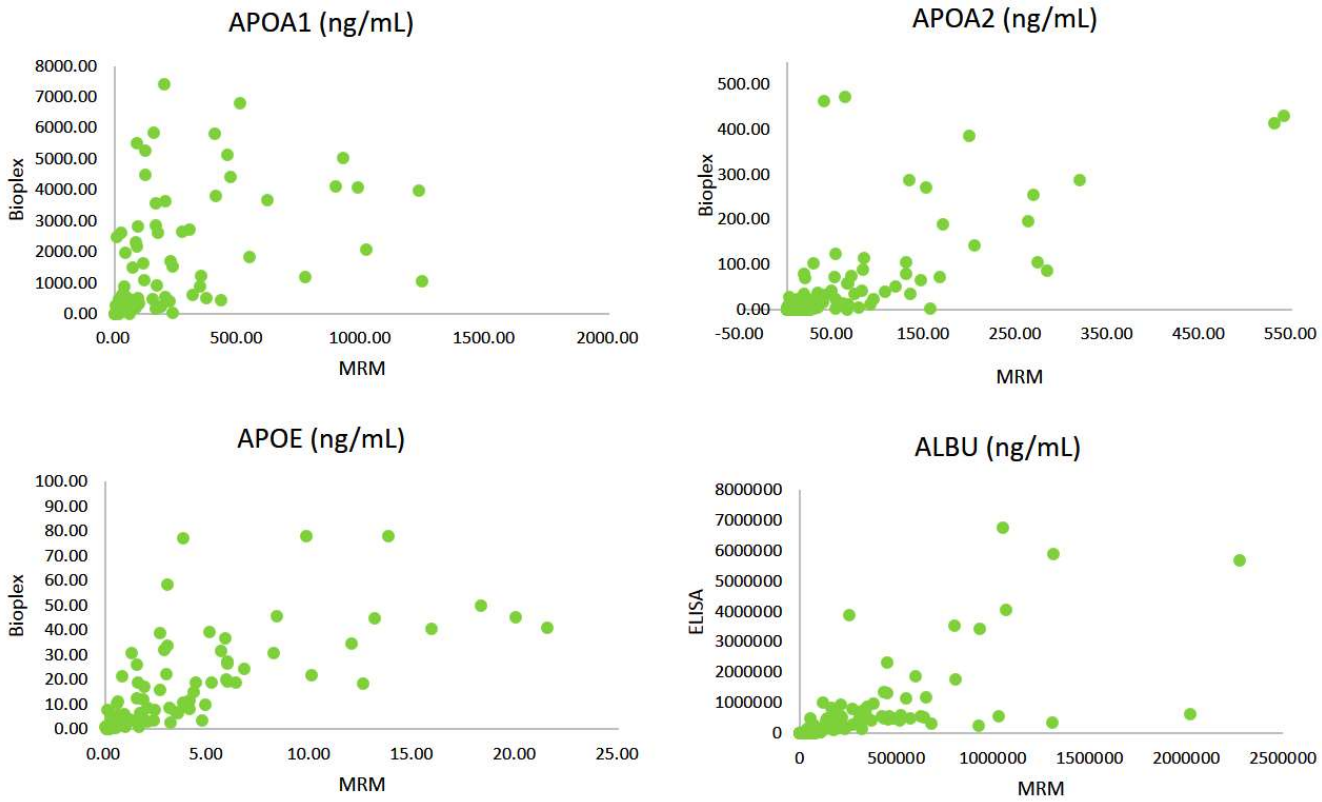

RBP
p < 0.001
149.0 : 608.0
SAA4
p < 0.001
14.5 : 85.7
THRB
p < 0.001
0.9 : 3.8
TRFE
p < 0.001
1621.8 : 7297.6
TSP1
p = 0.004
240.8 : 458.4
TTHY
p < 0.001
566.2 : 1819.4
VTDB
p < 0.001
252.5 : 1138.2
ZA2G
p = 0.102
7927.9 : 7597.5
Concentration (ng/mL)
Control
(N=58)
OSCC
(N=61)

Supplemental Figure S1E



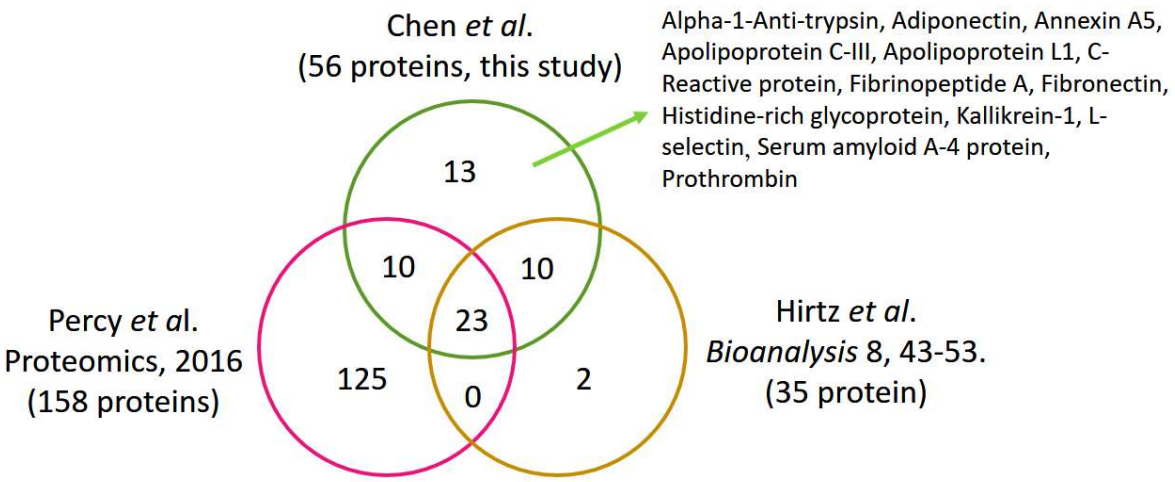

CFAH
AUC: 0.913
CFB
AUC: 0.854
CLUS
AUC: 0.671
CO3
AUC: 0.809
CO9
AUC: 0.704
CRP
AUC: 0.771
AUC: 0.831
FETUA
AUC: 0.855
FIBA
AUC: 0.739
FIBB
AUC: 0.828
FIBG
AUC: 0.609
FINC
AUC: 0.843
FPA
AUC: 0.487
GELS
AUC: 0.632
HEMO
AUC: 0.851
HEP2
AUC: 0.897
HPT
AUC: 0.791
HRG
AUC: 0.854
ITIH1
AUC: 0.854
KNG1
AUC: 0.830
PLMN
AUC: 0.819
Q9UJ43
AUC: 0.711
RBP
AUC: 0.790
SAA4
AUC: 0.757
SAMP
AUC: 0.884
THRB
AUC: 0.707
TRFE
AUC: 0.802
TSP1
AUC: 0.653
TTHY
AUC: 0.744
VTDB
AUC: 0.871
VTNC
AUC: 0.870
ZA2G
AUC: 0.587
Sensitivity
1-specificity

Supplemental Figure S2



		Spearman's correlation		
Protein name	Assays	Correlation (r)	Significance (p-value)	n
APOA1	MRM vs. BioPlex	0.792	< 0.001	117
APOA2	MRM vs. BioPlex	0.779	< 0.001	117
APOE	MRM vs. BioPlex	0.854	< 0.001	117
Albumin	MRM vs. ELISA	0.871	< 0.001	116

Supplemental Figure S3



Supplemental Table S1

Supplemental Table S1A: Demographic characteristics and intake of cigarette and betel nut (n=61) – clinical sample set 1

	Total (n=61)	Control (n=29)	OSCC (n=32)	*p*
Sex[1]				0.3371
Male	60	29	31	
Female	1	0	1	
Age[2]	49.8±10.5	48.3±11.9	51.1±9	0.2915
Smoke[2] (packs per day x years)	20.5±16.5	16.6±10.1	24.1±20.1	0.0677
Betel nut[2] (nuts per day x years)	204±227.9	97.9±109.6	300.1±263.8	0.0003

[1]Fisher's exact test.

[2]Analysis of variance (ANOVA).

Supplemental Table S1B: Demographic characteristics and intake of cigarette and betel nut (n=58) – Clinical sample set 2

	Total (n=58)	Control (n=29)	OSCC (n=29)	*p*
Sex[1]				0.1501
Male	56	27	29	
Female	2	2	0	
Age[2]	50.4±11.1	49.2±11.9	51.6±10.3	0.4024
Smoke[2] (packs per day x years)	21.9±22.4	15.6±13	28.3±27.8	0.0314
Betel nut[2] (nuts per day x years)	263.5±390.3	69.3±80.1	457.6±475	0.0002

[1]Fisher's exact test.

[2]Analysis of variance (ANOVA).

Supplemental Table S1C: Comparison between clinical sets: Demographic characteristics and intake of cigarette and betel nut

	sample set 1 (n=61)	sample set 2 (n=58)	*p*
Group			
Control	29	29	
OSCC	32	29	
Sex[1]			0.5292
Male	60	56	
Female	1	2	
Age[2]	49.8±10.5	50.4±11.1	0.7496
Smoke[2] (packs per day x years)	20.5±16.5	21.9±22.4	0.7097
Betel nut[2] (nuts per day x years)	204±227.9	263.5±390.3	0.3156

[1]Fisher's exact test.

[2]Analysis of variance (ANOVA).

Supplemental Table S2. MRM parameters of the 56 peptides used for quantitation of 56 proteins in saliva.

Gene Symbol	Protein	Peptide	Transition	Light		Heavy (SIS)		Collision Energy (V)	Retention Time (min)	quantifier peptide	Fixed SIS Peptide Concentration (fmol/ug total protein)
				Q1 *m/z*	Q3 *m/z*	Q1 *m/z*	Q3 *m/z*				
	ADIPO	IFYNQQNHYDGSTGK	3/y13(2+)	591.27	756.33	593.94	760.34	25	14.4	*	10
	ADIPO	IFYNQQNHYDGSTGK	3/y14(2+)	591.27	829.86	593.94	833.87	26	14.4		10
	ADIPO	IFYNQQNHYDGSTGK	3/y5	591.27	449.24	593.94	457.25	35.5	14.4		10
	AFAM	DADPDTFFAK	2/y7(2+)	563.76	413.21	567.76	417.4	25	26.5	*	10
	AFAM	DADPDTFFAK	2/y8(2+)	563.76	470.72	567.76	474.9	21	26.5		10
	AFAM	DADPDTFFAK	2/y5	563.76	613.33	567.76	621.5	30	26.5		10
	A1AT	LSITGTYDLK	2/y6	555.81	696.36	559.81	704.37	29	26.8	*	20
	A1AT	LSITGTYDLK	2/y7	555.81	797.4	559.81	805.42	26	26.8		20
	A1AT	LSITGTYDLK	2/y8	555.81	910.49	559.81	918.5	30	26.8		20
	FETUA	HTLNQIDEVK	2/y8	598.82	958.52	602.82	966.53	31	13.9		5
	FETUA	HTLNQIDEVK	3/y4	399.55	490.25	402.22	498.26	15	13.9	*	5
	FETUA	HTLNQIDEVK	3/b6(2+)	399.55	354.2	402.22	354.2	12	13.9		5
	ANGT	ALQDQLVLVAAK	2/y10(2+)	634.88	542.82	638.89	546.83	26.8	30.5	*	5

	ANGT	ALQDQLVLVAAK	2/y9	634.88	956.58	638.89	964.59	27.6	30.5		5
	ANGT	ALQDQLVLVAAK	2/y5	634.88	501.34	638.89	509.35	34	30.5		5
	ANXA5	GTVTDFPGFDER	2/y6	670.81	720.33	675.81	730.34	35.8	29	*	5
	ANXA5	GTVTDFPGFDER	2/y7	670.81	867.4	675.81	877.41	33.5	29		5
	ANXA5	GTVTDFPGFDER	2/b6	670.81	621.2	675.81	621.2	23	29		5
	APOA1	ATEHLSTLSEK	2/y6	608.31	664.35	612.32	672.37	34	10.7		50
	APOA1	ATEHLSTLSEK	3/y9(2+)	405.88	522.27	408.55	526.28	18	10.7	*	50
	APOA1	ATEHLSTLSEK	3/y5	405.88	577.32	408.55	585.33	17	10.7		50
	APOA2	SPELQAEAK	2/y8(2+)	486.75	443.24	490.76	447.24	26.7	9.4	*	10
	APOA2	SPELQAEAK	2/y5	486.75	546.29	490.76	554.3	27	9.4		10
	APOA2	SPELQAEAK	2/b7	486.75	755.36	490.76	755.36	21.8	9.4		10
	APOA4	SLAPYAQDTQEK	2/y9(2+)	675.83	540.25	679.84	544.4	28.2	14.5	*	2
	APOA4	SLAPYAQDTQEK	2/y7	675.83	819.38	679.84	827.4	40	14.5		2
	APOA4	SLAPYAQDTQEK	2/y10(2+)	675.83	575.77	679.84	579.8	29	14.5		2
	APOL1	VTEPISAESGEQVER	2/y12(2+)	815.9	651.32	820.9	656.5	39	17.7	*	10
	APOL1	VTEPISAESGEQVER	3/y6	544.27	717.35	547.6	727.36	27	17.7		10

	APOL1	VTEPISAESGEQVER	3/y7	544.27	804.38	547.6	814.39	26	17.7		10
	APOH	ATVVYQGER	2/y5	511.77	652.3	516.77	662.31	27.7	10.5		5
	APOH	ATVVYQGER	2/y6	511.77	751.37	516.77	761.38	26.4	10.5	*	5
	APOH	ATVVYQGER	2/y7	511.77	850.44	516.77	860.45	25.3	10.5		5
	CO9	TEHYEEQIEAFK	3/b7(2+)	508.57	459.19	511.24	459.19	21	22.2		20
	CO9	TEHYEEQIEAFK	3/b5	508.57	660.26	511.24	660.26	26	22.2	*	20
	CO9	TEHYEEQIEAFK	3/b6	508.57	789.3	511.24	789.3	25	22.2		20
	FIBB	QGFGNVATNTDGK	2/y7	654.81	706.34	658.82	714.35	34	14	*	50
	FIBB	QGFGNVATNTDGK	2/y8	654.81	805.41	658.82	813.42	34	14		50
	FIBB	QGFGNVATNTDGK	2/y5	654.81	534.25	658.82	542.3	37	14		50
	ITIH1	AAISGENAGLVR	2/y9	579.32	902.47	584.32	912.48	35	16.9	*	2
	ITIH1	AAISGENAGLVR	2/y8	579.32	815.44	584.32	825.45	33	16.9		2
	ITIH1	AAISGENAGLVR	2/y10(2+)	579.32	508.28	584.32	513.28	25	16.9		2
	PLMN	LFLEPTR	2/y5	438.25	615.35	443.26	625.35	20	23.5	*	2
	PLMN	LFLEPTR	2/y3	438.25	373.22	443.26	383.23	30	23.5		2
	PLMN	LFLEPTR	2/y4	438.25	502.26	443.26	512.27	24	23.5		2

	THRB	ETAASLLQAGYK	2/y6	626.33	679.38	630.34	687.39	28	25		5
	THRB	ETAASLLQAGYK	2/y8	626.33	879.49	630.34	887.51	29	25	*	5
	THRB	ETAASLLQAGYK	2/y5	626.33	566.29	630.34	574.31	27	25		5
	SAA4	GPGGVWAAK	2/y8(2+)	421.73	393.22	425.74	397.23	24	14.2	*	5
	SAA4	GPGGVWAAK	2/b8	421.73	696.37	425.74	696.37	23	14.2		5
	SAA4	GPGGVWAAK	2/y4	421.73	475.27	425.74	483.28	23.5	14.2		5
	TSP1	FVFGTTPEDILR	2/y10(2+)	697.87	574.8	702.87	579.81	28	39.9		5
	TSP1	FVFGTTPEDILR	2/y6	697.87	742.41	702.87	752.42	34	39.9	*	5
	TSP1	FVFGTTPEDILR	2/y9	697.87	1001.53	702.87	1011.53	36	39.9		5
	TRFE	EGYYGYTGAFR	2/y7	642.29	771.38	647.29	781.39	32.5	24.8	*	100
	TRFE	EGYYGYTGAFR	2/y5	642.29	551.29	647.29	561.3	31	24.8		100
	TRFE	EGYYGYTGAFR	2/y8	642.29	934.44	647.29	944.45	34	24.8		100
	A1AG1	NWGLSVYADKPETTK	3/y13(2+)	570.29	704.87	572.96	708.88	25	25.9	*	20
	A1AG1	NWGLSVYADKPETTK	3/b10(2+)	570.29	567.78	572.96	567.78	22	25.9		20
	A1AG1	NWGLSVYADKPETTK	3/y9	570.29	1052.53	572.96	1060.54	31	25.9		20
	A2MG	TEHPFTVEEFVLPK	3/y5	558.29	603.39	560.3	609.41	22.5	36		20

	A2MG	TEHPFTVEEFVLPK	3/y6	558.29	732.43	560.3	738.45	23	36	*	20
	A2MG	TEHPFTVEEFVLPK	3/b6	558.29	713.33	560.3	713.33	24	36		20
	ANT3	DDLYVSDAFHK	2/y9(2+)	437.21	540.28	439.88	544.29	17.7	23.5		10
	ANT3	DDLYVSDAFHK	2/y8(2+)	437.21	483.74	439.88	487.74	17.6	23.5		10
	ANT3	DDLYVSDAFHK	2/y6	437.21	704.34	439.88	712.35	23	23.5	*	10
	APOB	FPEVDVLTK	2/y8(2+)	524.29	450.76	528.3	454.76	27.4	30	*	2
	APOB	FPEVDVLTK	2/y6	524.29	674.41	528.3	682.42	32	30		2
	APOB	FPEVDVLTK	2/y7	524.29	803.45	528.3	811.47	28.9	30		2
	CERU	EYTDASFTNR	2/y5	602.27	624.31	607.27	634.32	29	15.6		5
	CERU	EYTDASFTNR	2/y4	602.27	537.28	607.27	547.29	29	15.6	*	5
	CERU	EYTDASFTNR	2/y8	602.27	911.42	607.27	921.43	37	15.6		5
	FIBA	GSESGIFTNTK	2/y5	570.78	610.32	574.79	618.33	28.7	15.8	*	5
	FIBA	GSESGIFTNTK	2/y7	570.78	780.43	574.79	788.44	28	15.8		5
	FIBA	GSESGIFTNTK	2/y8	570.78	867.46	574.79	875.47	27	15.8		5
	FIBG	DTVQIHDITGK	3/y9(2+)	409.55	505.79	412.22	509.79	17.8	17.8	*	2
	FIBG	DTVQIHDITGK	3/y8(2+)	409.55	456.25	412.22	460.26	16.5	17.8		2

	FIBG	DTVQIHDITGK	3/y6	409.55	670.35	412.22	678.37	22	17.8		2
	HEP2	TLEAQLTPR	2/y7	514.79	814.44	519.79	824.45	27	19.3	*	2
	HEP2	TLEAQLTPR	2/y6	514.79	685.4	519.79	695.41	27	19.3		2
	HEP2	TLEAQLTPR	2/y4	514.79	486.3	519.79	496.31	28	19.3		2
	TTHY	AADDTWEPFASGK	2/y6	697.81	606.32	701.82	614.34	38	27.9		20
	TTHY	AADDTWEPFASGK	2/y7	697.81	735.37	701.82	743.38	32	27.9		20
	TTHY	AADDTWEPFASGK	2/y8	697.81	921.45	701.82	929.46	36	27.9	*	20
	VTDB	THLPEVFLSK	2/b3	585.83	352.2	588.84	352.2	28	26.8		20
	VTDB	THLPEVFLSK	2/y7	585.83	819.46	588.84	825.48	32	26.8		20
	VTDB	THLPEVFLSK	2/y8	585.83	932.55	588.84	938.57	30	26.8	*	20
	ALBU	LVNEVTEFAK	2/y8	575.31	937.46	578.32	943.48	29	24.2		1000
	ALBU	LVNEVTEFAK	2/y6	575.31	694.38	578.32	700.4	28	24.2		1000
	ALBU	LVNEVTEFAK	2/y5	575.31	595.31	578.32	601.33	29	24.2	*	1000
	AACT	EIGELYLPK	2/y7	531.3	819.46	535.3	827.48	25.8	29		2
	AACT	EIGELYLPK	2/y5	531.3	633.4	535.3	641.41	21	29	*	2
	AACT	EIGELYLPK	2/y3	531.3	357.25	535.3	365.26	21	29		2

	A1BG	LETPDFQLFK	2/y7	619.33	894.47	623.33	902.49	28.6	38.1	*	10
	A1BG	LETPDFQLFK	2/y8(2+)	619.33	498.26	623.33	502.3	26	38.1		10
	A1BG	LETPDFQLFK	2/b3	619.33	344.18	623.33	344.18	25	38.1		10
	APOC1	TPDVSSALDK	2/y9(2+)	516.76	466.24	520.77	470.25	29	16.5		5
	APOC1	TPDVSSALDK	2/y6	516.76	620.32	520.77	628.34	29	16.5	*	5
	APOC1	TPDVSSALDK	2/y8	516.76	834.42	520.77	842.43	26	16.5		5
	APOC3	GWVTDGFSSLK	2/y8	598.8	854.43	602.81	862.44	25	32.9	*	5
	APOC3	GWVTDGFSSLK	2/y9	598.8	953.49	602.81	961.51	25	32.9		5
	APOC3	GWVTDGFSSLK	2/b3	598.8	343.18	602.81	343.18	22	32.9		5
	APOD	IPTTFENGR	2/y8(2+)	517.77	461.22	522.77	466.23	25	16	*	2
	APOD	IPTTFENGR	2/y6	517.77	723.34	522.77	733.35	31	16		2
	APOD	IPTTFENGR	2/y7	517.77	824.39	522.77	834.4	30	16		2
	APOE	LGPLVEQGR	2/y7(2+)	484.78	399.73	489.78	404.73	24	17	*	1
	APOE	LGPLVEQGR	2/y4	484.78	489.24	489.78	499.25	30	17		1
	APOE	LGPLVEQGR	2/y5	484.78	588.31	489.78	598.32	30	17		1
	CLUS	ELDESLQVAER	2/y5	644.82	602.33	649.83	612.33	29	21.4		10

	CLUS	ELDESLQVAER	2/y4	644.82	474.27	649.83	484.28	32	21.4		10
	CLUS	ELDESLQVAER	2/y3	644.82	375.2	649.83	385.21	27	21.4	*	10
	C1 inactivator	LLDSLPSDTR	2/y5	558.8	575.28	563.8	585.29	24	22	*	5
	C1 inactivator	LLDSLPSDTR	2/y8	558.8	890.42	563.8	900.43	28	22		5
	C1 inactivator	LLDSLPSDTR	2/b4	558.8	429.23	563.8	429.23	27	22		5
	CFB	EELLPAQDIK	2/y6	578.32	671.37	581.33	677.39	24	23.7	*	10
	CFB	EELLPAQDIK	2/y7	578.32	784.46	581.33	790.48	26	23.7		10
	CFB	EELLPAQDIK	2/y8	578.32	897.54	581.33	903.56	24	23.7		10
	CFAH	SPDVINGSPISQK	2/b4	671.35	399.19	674.36	399.19	34	19.7		2
	CFAH	SPDVINGSPISQK	2/y8	671.35	830.44	674.36	836.46	33	19.7	*	2
	CFAH	SPDVINGSPISQK	2/y9	671.35	943.52	674.36	949.54	35	19.7		2
	CRP	ESDTSYVSLK	2/y6	564.77	696.39	567.78	702.41	28	17.6		2
	CRP	ESDTSYVSLK	2/y5	564.77	609.36	567.78	615.38	24	17.6		2
	CRP	ESDTSYVSLK	2/y3	564.77	347.23	567.78	353.25	24	17.6	*	2
	A2AP	LGNQEPGGQTALK	2/y8	656.85	771.44	660.85	779.45	34	13.1	*	2

	A2AP	LGNQEPGGQTALK	2/b5	656.85	542.26	660.85	542.26	29	13.1		2
	A2AP	LGNQEPGGQTALK	2/y9	656.85	900.48	660.85	908.49	36	13.1		2
	GELS	TGAQELLR	2/y4	444.25	530.33	447.26	536.35	24	16		20
	GELS	TGAQELLR	2/y5	444.25	658.39	447.26	664.41	25	16	*	20
	GELS	TGAQELLR	2/y6	444.25	729.43	447.26	735.45	25	16		20
	KNG1	TVGSDTFYSFK	2/y9	626.3	1051.47	630.31	1059.49	27	27.1	*	5
	KNG1	TVGSDTFYSFK	2/y6	626.3	792.39	630.31	800.41	34.5	27.1		5
	KNG1	TVGSDTFYSFK	2/y7	626.3	907.42	630.31	915.43	27	27.1		5
	RBP	YWGVASFLQK	2/y8	599.82	849.48	603.82	857.5	30	38.6	*	10
	RBP	YWGVASFLQK	2/y6	599.82	693.39	603.82	701.41	27	38.6		10
	RBP	YWGVASFLQK	2/y5	599.82	622.36	603.82	630.37	31	38.6		10
	SAMP	VGEYSLYIGR	2/y6	578.8	708.4	583.81	718.41	33	26.4		5
	SAMP	VGEYSLYIGR	2/y4	578.8	508.29	583.81	518.3	27	26.4	*	5
	SAMP	VGEYSLYIGR	2/y7	578.8	871.47	583.81	881.48	30	26.4		5
	ZA2G	EIPAWVPFDPAAQITK	2/y14(2+)	891.97	770.91	894.98	773.92	35	45.2		100
	ZA2G	EIPAWVPFDPAAQITK	2/y10	891.97	1087.58	894.98	1093.6	40	45.2	*	100

	ZA2G	EIPAWVPFDPAAQITK	2/b6	891.97	696.37	894.98	696.37	34	45.2		100
	FA12	VVGGLVALR	2/y7	442.29	685.44	447.29	695.44	22	25	*	2
	FA12	VVGGLVALR	2/y4	442.29	458.31	447.29	468.32	22	25		2
	FA12	VVGGLVALR	2/y8	442.29	784.5	447.29	794.51	26	25		2
	CO3	TGLQEVEVK	2/y6	501.78	731.39	505.78	739.41	26	16.8	*	20
	CO3	TGLQEVEVK	2/y5	501.78	603.33	505.78	611.35	28	16.8		20
	CO3	TGLQEVEVK	2/y7(2+)	501.78	422.74	505.78	426.75	24	16.8		20
	FINC	VPGTSTSATLTGLTR	2/y14(2+)	731.4	681.86	736.4	686.87	39	24	*	5
	FINC	VPGTSTSATLTGLTR	2/y9	731.4	919.52	736.4	929.53	45	24		5
	FINC	VPGTSTSATLTGLTR	2/y11	731.4	1107.6	736.4	1117.61	43	24		5
	HPT	VGYVSGWGR	2/y5	490.75	562.27	495.76	572.28	26	20.9	*	100
	HPT	VGYVSGWGR	2/y6	490.75	661.34	495.76	671.35	26	20.9		100
	HPT	VGYVSGWGR	2/y4	490.75	475.24	495.76	485.25	21	20.9		100
	HEMO	NFPSPVDAAFR	2/y9(2+)	610.81	480.25	615.81	485.26	24	30.8	*	20
	HEMO	NFPSPVDAAFR	2/y7	610.81	775.41	615.81	785.42	32	30.8		20
	HEMO	NFPSPVDAAFR	2/y8	610.81	862.44	615.81	872.45	34	30.8		20

	HRG	DGYLFQLLR	2/y5	562.81	676.41	567.81	686.42	25	44.7	*	5
	HRG	DGYLFQLLR	2/y6	562.81	789.5	567.81	799.51	28	44.7		5
	HRG	DGYLFQLLR	2/b3	562.81	336.12	567.81	336.12	25	44.7		5
	Q9UJ43	AEIEYLEK	2/y6	497.76	794.43	501.77	802.44	21	19.4	*	2
	Q9UJ43	AEIEYLEK	2/y5	497.76	681.35	501.77	689.36	23	19.4		2
	Q9UJ43	AEIEYLEK	2/y4	497.76	552.3	501.77	560.32	30	19.4		2
	VTNC	FEDGVLDPDYPR	2/y5	711.83	647.31	716.83	657.32	44	27.7		5
	VTNC	FEDGVLDPDYPR	2/b5	711.83	548.24	716.83	548.24	28	27.7		5
	VTNC	FEDGVLDPDYPR	2/y7	711.83	875.43	716.83	885.43	32	27.7	*	5
	FPA	ADSGEGDFLAEGGGVR	2/y7	768.85	645.33	773.85	655.34	37	23.5	*	5
	FPA	ADSGEGDFLAEGGGVR	2/y5	768.85	445.25	773.85	455.26	40	23.5		5
	FPA	ADSGEGDFLAEGGGVR	2/y8	768.85	758.42	773.85	768.42	39	23.5		5

Supplemental Table S3. The disease associations of the target proteins

	Protein	Name	Disease/Literatures
1	A1AG1	Alpha-1-acid glycoprotein 1	cervical cancer [1], gastric cancer [2], breast cancer [3]
2	A1AT	Alpha-1-anti-trypsin	breast cancer [3]
3	A1BG	Alpha-1B-glycoprotein	non-small cell lung cancer [4]
4	A2AP	Alpha-2-antiplasmin	Thrombosis [5], bladder cancer [6]
5	A2MG	alpha-2-macroglobulin	hepatocellular carcinoma [7]
6	AACT	Alpha-1-antichymotrypsin	pancreatic cancer [8,9]
7	ADIPO	Adiponectin	breast cancer [10], Endometrial Cancer [10]
8	AFAM	Afamin	polycystic ovary syndrome [11], thyroid carcinoma [12], ovarian cancer [13]
9	ALBU	Albumin	colorectal cancer [14], lung cancer [15], bladder cancer [6]
10	ANGT	Angiotensinogen	colorectal cancer [16], colon cancer [17]
11	ANT3	Antithrombin-III	hepatocellular carcinoma [18], primary central nervous system lymphoma [19]
12	ANXA5	Annexin A5	prostate cancer [20], Glioblastoma multiforme [21]
13	APOA1	Apolipoprotein A1	bladder cancer [6,22], ovarian cancer [23]
14	APOA2	Apolipoprotein A-II precursor	bladder cancer [6,22,24], ovarian cancer [25]
15	APOA4	Apolipoprotein A-IV	cervical cancer [26], ovarian cancer [27]
16	APOB	Apolipoprotein B-100	bladder cancer [28,29], colorectal cancer [30]

17	APOC1	Apolipoprotein C-I lipoprotein	hepatitis C virus [31], ovarian cancer [25], stomach cancer [32]
18	APOC3	Apolipoprotein C-III	stomach cancer [32]
19	APOD	Apolipoprotein D	colorectal cancer [33], breast cancer [34]
20	APOE	Apolipoprotein E	colorectal cancer [16],
21	APOH	apolipoprotein H (beta-2-glycoprotein I)	breast cancer [35], non-small cell lung cancer [36]
22	APOL1	Apolipoprotein L1	kidney diseases [37,38], renal cancer [39]
23	C1 inactivator	Complement C1 inactivator	hepatocellular carcinoma [40], hereditary angioedema [41]
24	CERU	Ceruloplasmin	breast cancer [42], pancreatic cancer [43]
25	CFAH	Complement factor H	liver disease [44], squamous cell carcinoma [45], ovarian cancer [46]
26	CFB	Complement factor B	pancreatic ductal adenocarcinoma [47], nasopharyngeal carcinoma [48]
27	CLUS	Clusterin	hepatocellular carcinoma [49], esophageal cancer [50]
28	CO3	Complement C3	retinal degenerative diseases [51], neuroblastoma [52]
29	CO9	Complement C9	lung cancer [53]
30	CRP	C-Reactive protein	lung cancer [15], bladder cancer [6]
31	FA12	Coagulation factor XIIa LC	bladder cancer [6]
32	FETUA	alpha-2-HS-glycoprotein	cervical cancer[1], colorectal cancer [54]
33	FIBA	Fibrinogen alpha chain	bladder cancer [6]
34	FIBB	Fibrinogen beta chain	bladder cancer [6,55], oral squamous cell carcinoma [56]

35	FIBG	Fibrinogen gamma chain	prostate-, lung-, and breast-cancer [4], bladder cancer [6]
36	FINC	Fibronectin	Breast cancer [15,57]
37	FPA	Fibrinopeptide A	gastric cancer [58], non-alcoholic fatty liver disease [59]
38	GELS	Gelsolin, isoform 1	cervical cancer [60], liver and kidney toxicity [61]
39	HEMO	Hemopexin	IgA nephropathy [62], oral squamous cell carcinoma [63]
40	HEP2	Heparin cofactor II	mucopolysaccharidosis [64], bladder cancer [22]
41	HPT	Haptoglobin beta chain	cervical cancer[1], lung cancer [65]
42	HRG	Histidine-rich glycoprotein	breast cancer [66], colorectal cancer [67]
43	ITIH1	Inter-alpha-trypsin Inhibitor heavy chain 1	urothelial neoplasm [68], bladder cancer [6]
44	KNG1	Kininogen-1	colorectal cancer [69], gastric cancer [70]
45	PLMN	Plasminogen	cancer [71], gastric cancer [72]
46	Q9UJ43	L-selectin	bladder cancer [6,73]
47	RBP	Plasma retinol-binding protein	cardiovascular disease [74], ovarian cancer [75]
48	SAA4	Serum amyloid A-4 protein	bladder cancer [28], ovarian carcinomas [76]
49	SAMP	Serum amyloid P-component	acute myocardial infarction [77], kidney diseases [78]
50	THRB	Prothrombin	prostate cancer [79], hepatocellular carcinoma [80]
51	TRFE	Transferrin	colon cancer [81], ovarian cancer [82]
52	TSP1	Thrombospondin-1	pancreatic cancer [20], non-small cell lung cancer [83]

53	TTHY	Transthyretin	lung cancer and lung infection [84], pancreatic ductal adenocarcinoma [85]
54	VTDB	Vitamin D-binding protein	cervical cancer[1], colorectal cancer [16],
55	VTNC	Vitronectin	ovarian cancer [86], gastric adenocarcinoma [87]
56	ZA2G	Zinc-alpha-2-glycoprotein	colon cancer [88], prostate cancer [89], diabetic nephropathy [90]

Supplemental Table S4. LOD and LLOQ of the 56 salivary peptides determined using the standard saliva sample which was pooled equal amounts of proteins from three individuals.

LOD is defined as the lowest level in the calibration curve at which a signal is observed for the endogenous target in all three processed replicates with a signal to noise ratio (S/N) above 20:1. LLOQ is defined as the lowest concentration in the calibration curves of natural peptides which can be measured with S/N>20 and <20% CV in three processed replicates which were independently digested.

The LOD and LLOQ values are reported as injection amount on column (amol/μg total salivary protein). The LOD and LLOQ values are also reported as protein concentration (ng/mL) on the basis of average total salivary protein concentration (2013 μg/ml) of the standard saliva sample (sample I).

N/A: Not available from the analysis of standard urine sample with CV below 20% (n=3).

The protein concentration of each target is expressed in ng/ml of saliva, which is exactly the same as the determined level of the proteotypic peptide by assuming complete tryptic digestion (i.e., 100% recovery). 0.9 μg of tryptic peptides were injected on column for each LC-MRM-MS analysis.

Protein name	Ion transition	MW(Da)	SIS conc. (fmol/μg)	LOD			LLOQ		
				(amol/μg)	(ng/ml)	amounts injected on column (amol)	(amol/μg)	(ng/ml)	amounts injected on column (amol)
A1AG1	3/y13(2+)	23,512	20	5628.0	266.4	5065.2	5628.00	266.37	5065.2
A1AT	2/y6	46,737	20	654.8	61.6	589.3	654.78	61.60	589.3
A1BG	2/y7	54,254	10	0.2	0.0	0.2	84.24	9.20	75.8

A2AP	2/y8	54,566	2	4.3	0.5	3.9	8.55	0.94	7.7
A2MG	3/y6	163,291	20	2.9	0.9	2.6	143.28	47.10	129.0
AACT	2/y5	47,651	2	5.2	0.5	4.7	5.16	0.49	4.6
ADIPO	3/y13(2+)	26,414	10	11.5	0.6	10.4	22.98	1.22	20.7
AFAM	2/y7(2+)	69,069	10	38.1	5.3	34.3	380.70	52.93	342.6
ALBU	2/y5	69,367	1000	663.2	92.6	596.9	663.24	92.61	596.9
ANGT	2/y10(2+)	53,154	5	49.8	5.3	44.8	49.82	5.33	44.8
ANT3	2/y6	52,602	10	29.8	3.2	26.8	596.70	63.18	537.0
ANXA5	2/y6	35,937	5	19.5	1.4	17.6	19.50	1.41	17.6
APOA1	3/y9(2+)	30,778	50	52.7	3.3	47.4	52.70	3.26	47.4
APOA2	2/y8(2+)	11,175	10	22.8	0.5	20.5	227.99	5.13	205.2
APOA4	2/y9(2+)	45,399	2	10.9	1.0	9.8	43.60	3.98	39.2
APOB	2/y8(2+)	515,605	2	1.3	1.4	1.2	2.61	2.71	2.3
APOC1	2/y6	9,332	5	16.6	0.3	14.9	16.62	0.31	15.0
APOC3	2/y8	10,852	5	5.5	0.1	5.0	54.90	1.20	49.4
APOD	2/y8(2+)	21,276	2	5.8	0.2	5.2	116.73	5.00	105.1
APOE	2/y7(2+)	36,154	1	3.3	0.2	3.0	16.37	1.19	14.7

APOH	2/y6	38,298	5	44.6	3.4	40.1	44.56	3.44	40.1
APOL1	2/y12(2+)	43,974	10	180.0	15.9	162.0	900.00	79.67	810.0
C1 inactivator	2/y5	55,154	5	0.5	0.1	0.5	23.90	2.65	21.5
CERU	2/y4	122,205	5	107.5	26.4	96.8	107.49	26.44	96.7
CFAH	2/y8	139,096	2	12.2	3.4	11.0	24.37	6.82	21.9
CFB	2/y6	85,533	10	51.9	8.9	46.7	51.90	8.94	46.7
CLUS	2/y3	52,495	10	1.2	0.1	1.1	116.25	12.28	104.6
CO3	2/y6	187,148	20	173.3	65.3	156.0	173.34	65.30	156.0
CO9	3/b5	63,173	20	1110.0	141.2	999.0	1110.00	141.16	999.0
CRP	2/y3	25,039	2	22.6	1.1	20.3	225.90	11.39	203.3
FA12	2/y7	67,792	2	6.4	0.9	5.8	25.57	3.49	23.0
FETUA	3/y4	39,325	5	78.1	6.2	70.3	78.08	6.18	70.3
FIBA	2/y5	94,973	5	43.5	8.3	39.2	87.03	16.64	78.3
FIBB	2/y7	55,928	50	7.1	0.8	6.4	355.73	40.05	320.2
FIBG	3/y9(2+)	51,512	2	0.1	0.0	0.1	11.55	1.20	10.4
FINC	2/y14(2+)	262,625	5	23.4	12.4	21.1	46.89	24.79	42.2
FPA	2/y7	94,973	5	94.1	18.0	84.7	1882.50	359.90	1694.3

GELS	2/y5	85,698	20	117.2	20.2	105.5	117.15	20.21	105.5
HEMO	2/y9(2+)	51,676	20	7.6	0.8	6.8	377.79	39.30	340.0
HEP2	2/y7	57,071	2	4.1	0.5	3.7	20.64	2.37	18.6
HPT	2/y5	45,205	100	8.8	0.8	7.9	439.22	39.97	395.3
HRG	2/y5	59,578	5	32.0	3.8	28.8	32.00	3.84	28.8
ITIH1	2/y9	101,389	2	11.5	2.3	10.4	22.97	4.69	20.7
KNG1	2/y9	38,720	5	0.1	0.0	0.1	100.37	14.54	90.3
PLMN	2/y5	71,957	2	13.0	2.4	11.7	12.98	2.37	11.7
Q9UJ43	2/y6	42,187	2	22.3	1.9	20.1	44.57	3.79	40.1
RBP	2/y8	23,010	10	0.1	0.0	0.1	559.80	25.93	503.8
SAA4	2/y8(2+)	14,747	5	255.2	7.6	229.7	255.15	7.57	229.6
SAMP	2/y4	25,387	5	21.8	1.1	19.6	218.25	11.15	196.4
THRB	2/y8	70,037	5	39.9	5.6	35.9	N/A	N/A	N/A
TRFE	2/y7	77,064	100	681.2	105.7	613.1	681.15	105.67	613.0
TSP1	2/y6	129,383	5	9.8	2.6	8.8	49.20	12.81	44.3
TTHY	2/y8	15,887	20	413.3	13.2	372.0	413.34	13.22	372.0
VTDB	2/y8	52,964	20	72.8	7.8	65.5	72.81	7.76	65.5

VTNC	2/y7	54,306	5	2.5	0.3	2.3	246.47	26.94	221.8
ZA2G	2/y10	34,259	100	7.4	0.5	6.7	7428.00	512.26	6685.2

Supplemental Table S5. The average concentration of control and OSCCC patients. The data of clinical group 1 (n=61) and group 2 (n=58) are expressed as fmol/μg in (A) and (C) and ng/mL in (B) and (D). The data of all 119 individual samples are expressed as (E) fmol/μg and (F) ng/mL.

(A)

	Control (n=29)				OSCC (n=32)			
Protein	Concentration (fmol/μg)		Detectable case No.[a]	Quantifiable case No.[b]	Concentration (fmol/μg)		Detectable case No.[a]	Quantifiable case No.[b]
A1AG1	1.30 ±	1.38	(1/29)	(1/29)	2.29 ±	2.28	(2/32)	(2/32)
A1AT	13.04 ±	38.10	(25/29)	(25/29)	24.18 ±	34.58	(32/32)	(32/32)
A1BG	8.89 ±	7.48	(29/29)	(29/29)	22.06 ±	17.25	(32/32)	(32/32)
A2AP	0.21 ±	0.30	(28/29)	(28/29)	0.51 ±	0.60	(30/32)	(28/32)
A2MG	33.55 ±	31.98	(29/29)	(29/29)	63.06 ±	55.67	(32/32)	(32/32)
AACT	1.22 ±	2.80	(27/29)	(27/29)	2.86 ±	4.21	(32/32)	(32/32)
ADIPO	0.01 ±	0.02	(8/29)	(2/29)	0.03 ±	0.03	(22/32)	(16/32)
AFAM	0.58 ±	0.68	(29/29)	(13/29)	1.82 ±	1.30	(32/32)	(28/32)
ALBU	2034.41 ±	1773.94	(29/29)	(29/29)	4695.45 ±	2679.85	(32/32)	(32/32)
ANGT	0.89 ±	0.94	(26/29)	(26/29)	2.47 ±	1.46	(32/32)	(32/32)
ANT3	0.26 ±	0.36	(24/29)	(1/29)	1.00 ±	1.40	(32/32)	(14/32)

ANXA5	0.18 ±	0.15	(27/29)	(27/29)	0.65 ±	0.81	(30/32)	(30/32)
APOA1	8.47 ±	22.01	(28/29)	(28/29)	22.83 ±	45.26	(32/32)	(32/32)
APOA2	1.72 ±	3.26	(26/29)	(23/29)	5.86 ±	6.95	(29/32)	(28/32)
APOA4	0.17 ±	0.76	(11/29)	(7/29)	0.31 ±	0.55	(17/32)	(15/32)
APOB	0.03 ±	0.05	(27/29)	(24/29)	0.12 ±	0.15	(32/32)	(31/32)
APOC1	0.12 ±	0.15	(21/29)	(21/29)	0.22 ±	0.30	(30/32)	(30/32)
APOC3	0.13 ±	0.22	(27/29)	(12/29)	0.23 ±	0.43	(27/32)	(18/32)
APOD	0.37 ±	0.59	(18/29)	(13/29)	0.83 ±	0.82	(24/32)	(21/32)
APOE	0.06 ±	0.11	(29/29)	(20/29)	0.10 ±	0.16	(32/32)	(25/32)
APOH	2.78 ±	2.49	(29/29)	(29/29)	11.00 ±	6.98	(32/32)	(32/32)
APOL1	0.21 ±	0.21	(13/29)	(1/29)	0.43 ±	0.50	(23/32)	(5/32)
C1 inactivator	0.36 ±	0.52	(29/29)	(25/29)	1.00 ±	0.94	(32/32)	(31/32)
CERU	1.50 ±	1.27	(24/29)	(24/29)	4.74 ±	3.62	(32/32)	(32/32)
CFAH	0.33 ±	0.23	(29/29)	(28/29)	2.63 ±	1.95	(32/32)	(32/32)
CFB	0.71 ±	0.61	(25/29)	(25/29)	2.22 ±	1.97	(32/32)	(32/32)
CLUS	12.13 ±	7.72	(29/29)	(29/29)	16.51 ±	12.73	(32/32)	(32/32)
CO3	9.30 ±	6.79	(27/29)	(27/29)	20.47 ±	12.32	(32/32)	(32/32)

CO9	0.18 ±	0.16	(0/29)	(0/29)	0.46 ±	0.66	(4/32)	(4/32)
CRP	0.03 ±	0.03	(9/29)	(0/29)	0.18 ±	0.28	(23/32)	(5/32)
FA12	0.06 ±	0.07	(28/29)	(18/29)	0.29 ±	0.31	(32/32)	(30/32)
FETUA	0.93 ±	0.92	(25/29)	(25/29)	4.37 ±	3.64	(30/32)	(30/32)
FIBA	0.31 ±	0.69	(18/29)	(14/29)	2.60 ±	4.94	(25/32)	(23/32)
FIBB	5.09 ±	4.51	(29/29)	(22/29)	22.18 ±	18.59	(32/32)	(30/32)
FIBG	0.00 ±	0.01	(13/29)	(2/29)	0.02 ±	0.03	(28/32)	(11/32)
FINC	0.49 ±	0.68	(21/29)	(21/29)	2.35 ±	2.42	(29/32)	(28/32)
FPA	0.39 ±	0.34	(24/29)	(0/29)	0.45 ±	1.21	(13/32)	(1/32)
GELS	23.29 ±	21.75	(29/29)	(29/29)	18.74 ±	9.53	(32/32)	(32/32)
HEMO	29.54 ±	33.46	(29/29)	(29/29)	92.19 ±	58.37	(32/32)	(32/32)
HEP2	0.16 ±	0.19	(28/29)	(28/29)	0.80 ±	0.76	(32/32)	(32/32)
HPT	212.25 ±	235.15	(29/29)	(29/29)	652.44 ±	524.99	(32/32)	(32/32)
HRG	1.53 ±	1.50	(29/29)	(29/29)	5.43 ±	5.40	(32/32)	(32/32)
ITIH1	0.48 ±	0.54	(29/29)	(29/29)	1.92 ±	1.79	(32/32)	(32/32)
KNG1	2.93 ±	2.79	(29/29)	(26/29)	9.23 ±	5.75	(32/32)	(32/32)
PLMN	0.05 ±	0.06	(21/29)	(21/29)	0.15 ±	0.13	(31/32)	(31/32)

Q9UJ43	0.11 ±	0.17	(12/29)	(12/29)	0.21 ±	0.20	(24/32)	(23/32)
RBP	9.72 ±	8.38	(29/29)	(29/29)	20.74 ±	16.77	(32/32)	(32/32)
SAA4	1.57 ±	3.11	(20/29)	(20/29)	5.32 ±	7.39	(25/32)	(25/32)
SAMP	0.14 ±	0.19	(27/29)	(6/29)	0.74 ±	0.80	(32/32)	(26/32)
THRB	0.01 ±	0.01	(1/29)	(0/29)	0.03 ±	0.04	(6/32)	(0/32)
TRFE	22.97 ±	21.08	(26/29)	(26/29)	51.75 ±	29.90	(32/32)	(32/32)
TSP1	1.75 ±	1.82	(29/29)	(29/29)	2.37 ±	2.66	(31/32)	(31/32)
TTHY	54.22 ±	45.41	(29/29)	(29/29)	97.14 ±	76.35	(32/32)	(32/32)
VTDB	4.99 ±	3.39	(29/29)	(29/29)	13.84 ±	8.43	(32/32)	(32/32)
VTNC	1.08 ±	1.82	(17/29)	(14/29)	3.16 ±	2.07	(32/32)	(31/32)
ZA2G	377.78 ±	285.86	(29/29)	(29/29)	257.40 ±	147.70	(32/32)	(32/32)

[a]: The LOD concentration is determined using the calibration curve with S/N>20. A sample with a protein concentration higher than its corresponding LOD value is defined as “Detectable” case for the protein.

[b]: The LLOQ concentration is determined using the calibration curve with S/N>20 and CV <20% CV in three replicates. A sample with a protein concentration higher than its corresponding LLOQ value is defined as “Quantifiable” case for the protein.

(B)

	Control (n=29)		OSCC (n=32)	
Protein	Concentration (ng/mL)		Concentration (ng/mL)	
A1AG1	33.28 ±	37.23	81.04 ±	97.17
A1AT	543.07 ±	1544.62	1758.60 ±	3537.29
A1BG	481.15 ±	395.58	1713.31 ±	2004.16
A2AP	11.56 ±	15.28	43.26 ±	68.75
A2MG	5726.74 ±	5965.82	14668.31 ±	16736.19
AACT	60.30 ±	127.63	175.16 ±	300.94
ADIPO	0.29 ±	0.50	1.46 ±	2.42
AFAM	41.87 ±	56.20	183.15 ±	171.19
ALBU	143641.13 ±	145125.96	483893.48 ±	429197.66
ANGT	48.84 ±	52.55	203.21 ±	182.94
ANT3	14.07 ±	17.99	85.05 ±	166.13
ANXA5	6.71 ±	6.73	30.34 ±	39.57
APOA1	250.99 ±	593.70	1278.37 ±	3114.08
APOA2	19.75 ±	33.92	99.41 ±	165.28
APOA4	7.26 ±	30.42	21.13 ±	42.60
APOB	14.81 ±	28.80	98.10 ±	128.68
APOC1	1.15 ±	1.58	3.32 ±	5.19
APOC3	1.47 ±	2.22	3.86 ±	8.09
APOD	7.43 ±	11.84	30.13 ±	38.80
APOE	2.34 ±	3.63	5.83 ±	11.79
APOH	113.04 ±	107.34	602.11 ±	533.83
APOL1	9.81 ±	9.46	29.47 ±	45.80
C1 inactivator	19.64 ±	27.11	74.85 ±	78.50
CERU	176.97 ±	157.15	850.36 ±	915.91

CFAH	54.41 ±	71.63	549.24 ±	600.94
CFB	63.29 ±	64.60	285.63 ±	322.31
CLUS	747.37 ±	741.67	1286.90 ±	1203.36
CO3	1777.47 ±	1541.32	5916.85 ±	5093.06
CO9	11.77 ±	11.16	41.23 ±	63.64
CRP	0.74 ±	0.97	6.38 ±	11.21
FA12	4.15 ±	4.26	31.28 ±	47.04
FETUA	45.27 ±	62.96	275.25 ±	349.67
FIBA	33.83 ±	66.39	355.25 ±	798.33
FIBB	315.02 ±	349.79	1952.38 ±	2150.04
FIBG	0.20 ±	0.59	1.37 ±	3.39
FINC	115.81 ±	150.99	954.65 ±	1449.58
FPA	40.40 ±	40.45	61.49 ±	147.43
GELS	2253.27 ±	2639.18	2609.78 ±	2772.53
HEMO	1570.68 ±	1813.75	7012.91 ±	6737.99
HEP2	8.68 ±	9.52	70.56 ±	92.74
HPT	9375.74 ±	9181.16	46882.78 ±	46925.97
HRG	95.40 ±	112.75	456.21 ±	628.46
ITIH1	49.74 ±	52.69	292.93 ±	382.55
KNG1	218.13 ±	239.91	1013.00 ±	986.62
PLMN	4.76 ±	5.72	20.78 ±	25.35
Q9UJ43	5.10 ±	10.76	13.46 ±	14.91
RBP	234.15 ±	236.57	740.74 ±	929.69
SAA4	22.12 ±	39.81	128.44 ±	218.69
SAMP	3.27 ±	3.46	22.84 ±	21.18
THRB	0.74 ±	0.80	2.47 ±	3.42
TRFE	1907.94 ±	2162.66	6197.51 ±	5843.15
TSP1	321.42 ±	539.21	458.19 ±	643.89

TTHY	928.43 ±	962.84	2405.03 ±	2548.05
VTDB	266.80 ±	218.23	1098.77 ±	1104.40
VTNC	55.38 ±	132.28	253.80 ±	243.45
ZA2G	14303.24 ±	14270.59	11206.80 ±	7325.05

(C)

Protein	Control (n=29) Concentration (fmol/μg)		Detectable case No.[a]	Quantifiable case No.[b]	OSCC (n=29) Concentration (fmol/μg)		Detectable case No.[a]	Quantifiable case No.[b]
A1AG1	0.61 ±	0.80	(0/29)	(0/29)	0.81 ±	0.59	(0/29)	(0/29)
A1AT	4.46 ±	13.18	(22/29)	(22/29)	47.76 ±	91.09	(29/29)	(29/29)
A1BG	6.06 ±	5.35	(29/29)	(29/29)	21.55 ±	22.96	(29/29)	(29/29)
A2AP	0.28 ±	0.66	(28/29)	(28/29)	0.94 ±	1.89	(26/29)	(25/29)
A2MG	13.54 ±	26.36	(29/29)	(24/29)	53.40 ±	53.61	(29/29)	(29/29)
AACT	0.70 ±	1.74	(26/29)	(26/29)	4.28 ±	6.08	(28/29)	(28/29)
ADIPO	0.01 ±	0.02	(9/29)	(3/29)	0.02 ±	0.02	(14/29)	(7/29)
AFAM	0.63 ±	0.86	(26/29)	(13/29)	1.42 ±	1.48	(29/29)	(24/29)
ALBU	1278.96 ±	1718.91	(29/29)	(29/29)	3607.52 ±	2633.84	(29/29)	(29/29)
ANGT	0.94 ±	1.43	(20/29)	(20/29)	3.10 ±	2.93	(29/29)	(29/29)
ANT3	0.14 ±	0.30	(14/29)	(3/29)	0.61 ±	0.79	(25/29)	(10/29)
ANXA5	0.31 ±	0.46	(25/29)	(25/29)	1.05 ±	2.21	(25/29)	(25/29)
APOA1	15.59 ±	48.16	(28/29)	(28/29)	60.50 ±	104.58	(29/29)	(29/29)

APOA2	2.20 ±	4.63	(23/29)	(17/29)	7.96 ±	10.41	(28/29)	(26/29)
APOA4	0.12 ±	0.48	(6/29)	(6/29)	0.88 ±	3.44	(17/29)	(14/29)
APOB	0.03 ±	0.06	(23/29)	(17/29)	0.20 ±	0.39	(29/29)	(29/29)
APOC1	0.12 ±	0.25	(18/29)	(18/29)	0.35 ±	0.43	(25/29)	(25/29)
APOC3	0.07 ±	0.17	(18/29)	(7/29)	0.23 ±	0.43	(21/29)	(13/29)
APOD	0.01 ±	0.02	(3/29)	(0/29)	0.16 ±	0.36	(11/29)	(9/29)
APOE	0.07 ±	0.10	(28/29)	(20/29)	0.25 ±	0.44	(29/29)	(22/29)
APOH	3.28 ±	3.24	(29/29)	(29/29)	10.53 ±	9.02	(29/29)	(29/29)
APOL1	0.19 ±	0.27	(10/29)	(1/29)	0.59 ±	0.89	(19/29)	(4/29)
C1 inactivator	0.25 ±	0.43	(29/29)	(17/29)	2.05 ±	2.32	(29/29)	(28/29)
CERU	0.98 ±	1.02	(22/29)	(22/29)	5.36 ±	5.19	(28/29)	(28/29)
CFAH	0.35 ±	0.49	(28/29)	(28/29)	2.61 ±	2.74	(29/29)	(29/29)
CFB	0.49 ±	0.52	(21/29)	(21/29)	3.04 ±	2.55	(29/29)	(29/29)
CLUS	10.39 ±	8.15	(29/29)	(29/29)	16.03 ±	11.52	(29/29)	(29/29)
CO3	7.67 ±	8.25	(25/29)	(25/29)	29.46 ±	23.00	(29/29)	(29/29)
CO9	0.14 ±	0.22	(1/29)	(1/29)	0.74 ±	1.37	(3/29)	(3/29)
CRP	0.03 ±	0.05	(12/29)	(1/29)	0.57 ±	1.38	(21/29)	(9/29)

FA12	0.10 ±	0.17	(28/29)	(19/29)	0.38 ±	0.51	(29/29)	(27/29)
FETUA	1.02 ±	1.65	(18/29)	(18/29)	5.29 ±	4.68	(29/29)	(29/29)
FIBA	1.51 ±	4.66	(18/29)	(12/29)	8.08 ±	21.36	(25/29)	(23/29)
FIBB	4.36 ±	5.94	(27/29)	(17/29)	25.85 ±	24.82	(29/29)	(28/29)
FIBG	0.01 ±	0.03	(15/29)	(5/29)	0.00 ±	0.00	(10/29)	(1/29)
FINC	0.35 ±	0.65	(16/29)	(16/29)	3.51 ±	3.80	(26/29)	(26/29)
FPA	1.22 ±	2.62	(18/29)	(4/29)	3.92 ±	8.31	(20/29)	(9/29)
GELS	16.46 ±	17.97	(29/29)	(29/29)	19.96 ±	11.79	(29/29)	(29/29)
HEMO	16.45 ±	21.13	(29/29)	(27/29)	68.37 ±	52.93	(29/29)	(29/29)
HEP2	0.21 ±	0.43	(29/29)	(27/29)	1.39 ±	1.84	(29/29)	(29/29)
HPT	63.81 ±	70.99	(29/29)	(29/29)	275.62 ±	292.19	(29/29)	(29/29)
HRG	0.93 ±	0.87	(29/29)	(29/29)	3.76 ±	2.51	(29/29)	(29/29)
ITIH1	0.65 ±	1.03	(27/29)	(27/29)	2.87 ±	3.76	(29/29)	(29/29)
KNG1	2.91 ±	4.59	(29/29)	(22/29)	9.14 ±	8.53	(29/29)	(29/29)
PLMN	0.05 ±	0.09	(16/29)	(16/29)	0.19 ±	0.22	(27/29)	(27/29)
Q9UJ43	0.15 ±	0.27	(11/29)	(11/29)	0.29 ±	0.32	(21/29)	(20/29)
RBP	2.91 ±	2.91	(29/29)	(22/29)	11.22 ±	11.07	(29/29)	(29/29)

SAA4	0.40 ±	0.79	(9/29)	(9/29)	1.65 ±	2.34	(23/29)	(23/29)
SAMP	0.07 ±	0.06	(23/29)	(1/29)	0.52 ±	0.65	(28/29)	(18/29)
THRB	0.02 ±	0.02	(2/29)	(0/29)	0.06 ±	0.11	(9/29)	(0/29)
TRFE	19.62 ±	24.18	(22/29)	(22/29)	67.47 ±	56.48	(28/29)	(28/29)
TSP1	1.05 ±	1.04	(29/29)	(26/29)	2.13 ±	2.03	(29/29)	(28/29)
TTHY	13.34 ±	12.29	(29/29)	(29/29)	44.52 ±	37.26	(29/29)	(29/29)
VTDB	4.72 ±	4.07	(29/29)	(29/29)	14.15 ±	8.81	(29/29)	(29/29)
VTNC	0.83 ±	1.19	(24/29)	(13/29)	6.25 ±	6.66	(29/29)	(25/29)
ZA2G	56.23 ±	56.97	(29/29)	(19/29)	73.80 ±	58.00	(29/29)	(26/29)

(D)

	Control (n=29)		OSCC (n=29)	
Protein	Concentration (ng/mL)		Concentration (ng/mL)	
A1AG1	12.77 ±	17.88	27.79 ±	28.71
A1AT	221.08 ±	728.48	3156.15 ±	6703.26
A1BG	323.71 ±	341.75	1903.15 ±	2727.02
A2AP	16.12 ±	42.44	71.89 ±	158.49
A2MG	2093.66 ±	4261.13	15351.89 ±	23272.10
AACT	32.71 ±	92.25	334.98 ±	553.38
ADIPO	0.32 ±	0.50	0.81 ±	1.38
AFAM	44.13 ±	70.68	154.07 ±	275.69
ALBU	81472.10 ±	128570.97	394896.34 ±	490580.28
ANGT	47.75 ±	78.72	286.96 ±	364.28
ANT3	7.20 ±	17.74	46.57 ±	61.00
ANXA5	9.69 ±	16.06	30.03 ±	51.93
APOA1	535.79 ±	1760.90	2738.90 ±	5213.57
APOA2	27.47 ±	60.69	127.92 ±	191.44
APOA4	6.08 ±	25.68	61.83 ±	253.84
APOB	18.77 ±	39.63	156.75 ±	341.97
APOC1	1.04 ±	2.74	4.45 ±	7.00
APOC3	0.79 ±	2.06	3.33 ±	7.20
APOD	0.10 ±	0.34	4.93 ±	9.13
APOE	2.60 ±	4.45	13.49 ±	26.65
APOH	125.66 ±	139.61	657.06 ±	823.55
APOL1	8.36 ±	13.90	36.69 ±	62.16
C1 inactivator	13.42 ±	26.90	170.32 ±	222.07
CERU	101.61 ±	110.36	1006.69 ±	1369.40

CFAH	48.33 ±	79.92	583.22 ±	929.87
CFB	37.95 ±	45.36	401.41 ±	521.77
CLUS	568.37 ±	679.94	1404.48 ±	1571.42
CO3	1285.63 ±	1516.91	8592.00 ±	10172.38
CO9	9.07 ±	16.62	79.75 ±	161.98
CRP	0.82 ±	1.33	29.38 ±	88.54
FA12	6.74 ±	13.52	39.83 ±	66.26
FETUA	34.99 ±	61.55	325.51 ±	396.95
FIBA	158.56 ±	449.27	1037.45 ±	3313.15
FIBB	227.15 ±	328.76	2362.68 ±	3231.79
FIBG	0.63 ±	1.45	0.12 ±	0.25
FINC	87.54 ±	194.01	1405.61 ±	2136.01
FPA	138.85 ±	332.53	471.85 ±	1078.67
GELS	1208.96 ±	1372.87	2825.18 ±	3415.41
HEMO	802.10 ±	1132.76	5643.09 ±	6898.71
HEP2	12.52 ±	29.60	114.51 ±	175.19
HPT	3047.84 ±	5204.47	21413.76 ±	34303.99
HRG	52.73 ±	61.08	334.53 ±	349.57
ITIH1	67.84 ±	126.91	479.10 ±	844.98
KNG1	201.54 ±	341.47	1087.91 ±	1505.63
PLMN	4.67 ±	9.26	27.06 ±	36.19
Q9UJ43	5.63 ±	11.29	20.24 ±	28.31
RBP	63.93 ±	72.49	461.62 ±	731.34
SAA4	6.80 ±	16.52	38.49 ±	73.74
SAMP	1.44 ±	1.22	15.15 ±	15.10
THRB	1.06 ±	1.30	5.32 ±	11.87
TRFE	1335.62 ±	1845.56	8511.40 ±	11693.74
TSP1	160.25 ±	226.96	458.54 ±	663.56

TTHY	204.05 ±	227.45	1173.08 ±	1572.67
VTDB	238.16 ±	237.40	1181.79 ±	1419.26
VTNC	45.54 ±	75.54	546.36 ±	861.29
ZA2G	1552.52 ±	1561.56	3614.73 ±	4405.75

(E)

	Control (n=58)				OSCC (n=61)			
Protein	Concentration (fmol/μg)		Detectable case No.[a]	Quantifiable case No.[b]	Concentration (fmol/μg)		Detectable case No.[a]	Quantifiable case No.[b]
A1AG1	0.96 ±	1.17	(1/58)	(1/58)	1.59 ±	1.84	(2/61)	(2/61)
A1AT	8.75 ±	28.59	(47/58)	(47/58)	35.39 ±	68.05	(61/61)	(61/61)
A1BG	7.47 ±	6.60	(58/58)	(58/58)	21.82 ±	19.99	(61/61)	(61/61)
A2AP	0.24 ±	0.51	(56/58)	(56/58)	0.72 ±	1.38	(56/61)	(53/61)
A2MG	23.55 ±	30.75	(58/58)	(53/58)	58.47 ±	54.46	(61/61)	(61/61)
AACT	0.96 ±	2.32	(53/58)	(53/58)	3.54 ±	5.19	(60/61)	(60/61)
ADIPO	0.01 ±	0.02	(17/58)	(5/58)	0.02 ±	0.03	(36/61)	(23/61)
AFAM	0.61 ±	0.77	(55/58)	(26/58)	1.63 ±	1.39	(61/61)	(52/61)
ALBU	1656.68 ±	1772.69	(58/58)	(58/58)	4178.24 ±	2692.20	(61/61)	(61/61)
ANGT	0.92 ±	1.20	(46/58)	(46/58)	2.77 ±	2.28	(61/61)	(61/61)
ANT3	0.20 ±	0.34	(38/58)	(4/58)	0.81 ±	1.16	(57/61)	(24/61)
ANXA5	0.25 ±	0.35	(52/58)	(52/58)	0.84 ±	1.63	(55/61)	(55/61)
APOA1	12.03 ±	37.29	(56/58)	(56/58)	40.74 ±	80.76	(61/61)	(61/61)

APOA2	1.96 ±	3.97	(49/58)	(40/58)	6.86 ±	8.76	(57/61)	(54/61)
APOA4	0.15 ±	0.63	(17/58)	(13/58)	0.58 ±	2.40	(34/61)	(29/61)
APOB	0.03 ±	0.06	(50/58)	(41/58)	0.16 ±	0.29	(61/61)	(60/61)
APOC1	0.12 ±	0.21	(39/58)	(39/58)	0.28 ±	0.37	(55/61)	(55/61)
APOC3	0.10 ±	0.20	(45/58)	(19/58)	0.23 ±	0.43	(48/61)	(31/61)
APOD	0.19 ±	0.45	(21/58)	(13/58)	0.51 ±	0.72	(35/61)	(30/61)
APOE	0.06 ±	0.10	(57/58)	(40/58)	0.17 ±	0.33	(61/61)	(47/61)
APOH	3.03 ±	2.88	(58/58)	(58/58)	10.77 ±	7.95	(61/61)	(61/61)
APOL1	0.20 ±	0.24	(23/58)	(2/58)	0.51 ±	0.71	(42/61)	(9/61)
C1 inactivator	0.30 ±	0.48	(58/58)	(42/58)	1.50 ±	1.80	(61/61)	(59/61)
CERU	1.24 ±	1.17	(46/58)	(46/58)	5.04 ±	4.41	(60/61)	(60/61)
CFAH	0.34 ±	0.38	(57/58)	(56/58)	2.62 ±	2.34	(61/61)	(61/61)
CFB	0.60 ±	0.57	(46/58)	(46/58)	2.61 ±	2.28	(61/61)	(61/61)
CLUS	11.26 ±	7.92	(58/58)	(58/58)	16.28 ±	12.07	(61/61)	(61/61)
CO3	8.48 ±	7.54	(52/58)	(52/58)	24.75 ±	18.59	(61/61)	(61/61)
CO9	0.16 ±	0.19	(1/58)	(1/58)	0.60 ±	1.06	(7/61)	(7/61)
CRP	0.03 ±	0.04	(21/58)	(1/58)	0.37 ±	0.99	(44/61)	(14/61)

FA12	0.08 ±	0.13	(56/58)	(37/58)	0.33 ±	0.41	(61/61)	(57/61)
FETUA	0.98 ±	1.32	(43/58)	(43/58)	4.80 ±	4.16	(59/61)	(59/61)
FIBA	0.91 ±	3.36	(36/58)	(26/58)	5.21 ±	15.27	(50/61)	(46/61)
FIBB	4.73 ±	5.24	(56/58)	(39/58)	23.93 ±	21.67	(61/61)	(58/61)
FIBG	0.01 ±	0.02	(28/58)	(7/58)	0.01 ±	0.02	(38/61)	(12/61)
FINC	0.42 ±	0.66	(37/58)	(37/58)	2.90 ±	3.18	(55/61)	(54/61)
FPA	0.80 ±	1.90	(42/58)	(4/58)	2.10 ±	6.00	(33/61)	(10/61)
GELS	19.88 ±	20.07	(58/58)	(58/58)	19.32 ±	10.59	(61/61)	(61/61)
HEMO	22.99 ±	28.51	(58/58)	(56/58)	80.87 ±	56.67	(61/61)	(61/61)
HEP2	0.18 ±	0.33	(57/58)	(55/58)	1.08 ±	1.41	(61/61)	(61/61)
HPT	138.03 ±	187.73	(58/58)	(58/58)	473.30 ±	467.17	(61/61)	(61/61)
HRG	1.23 ±	1.25	(58/58)	(58/58)	4.63 ±	4.33	(61/61)	(61/61)
ITIH1	0.57 ±	0.82	(56/58)	(56/58)	2.37 ±	2.91	(61/61)	(61/61)
KNG1	2.92 ±	3.76	(58/58)	(48/58)	9.19 ±	7.14	(61/61)	(61/61)
PLMN	0.05 ±	0.08	(37/58)	(37/58)	0.17 ±	0.18	(58/61)	(58/61)
Q9UJ43	0.13 ±	0.22	(23/58)	(23/58)	0.25 ±	0.27	(45/61)	(43/61)
RBP	6.31 ±	7.11	(58/58)	(51/58)	16.21 ±	15.02	(61/61)	(61/61)

SAA4	0.98 ±	2.32	(29/58)	(29/58)	3.58 ±	5.85	(48/61)	(48/61)
SAMP	0.10 ±	0.14	(50/58)	(7/58)	0.63 ±	0.74	(60/61)	(44/61)
THRB	0.01 ±	0.01	(3/58)	(0/58)	0.04 ±	0.08	(15/61)	(0/61)
TRFE	21.30 ±	22.55	(48/58)	(48/58)	59.22 ±	44.87	(60/61)	(60/61)
TSP1	1.40 ±	1.51	(58/58)	(55/58)	2.26 ±	2.36	(60/61)	(59/61)
TTHY	33.78 ±	38.89	(58/58)	(58/58)	72.12 ±	66.05	(61/61)	(61/61)
VTDB	4.86 ±	3.71	(58/58)	(58/58)	13.99 ±	8.54	(61/61)	(61/61)
VTNC	0.96 ±	1.53	(41/58)	(27/58)	4.63 ±	5.03	(61/61)	(56/61)
ZA2G	217.00 ±	260.84	(58/58)	(48/58)	170.11 ±	146.25	(61/61)	(58/61)

(F)

	Control (n=58)		OSCC (n=61)	
Protein	Concentration (ng/mL)		Concentration (ng/mL)	
A1AG1	23.03 ±	30.74	55.73 ±	77.35
A1AT	382.08 ±	1207.91	2423.01 ±	5284.79
A1BG	402.43 ±	374.89	1803.56 ±	2356.87
A2AP	13.84 ±	31.70	56.87 ±	119.89
A2MG	3910.20 ±	5455.30	14993.29 ±	19939.39
AACT	46.51 ±	111.25	251.14 ±	442.91
ADIPO	0.30 ±	0.50	1.15 ±	2.00
AFAM	43.00 ±	63.30	169.32 ±	225.44
ALBU	112556.62 ±	139461.33	441583.36 ±	457707.28
ANGT	48.30 ±	66.34	243.03 ±	284.60
ANT3	10.63 ±	18.04	66.75 ±	127.95
ANXA5	8.20 ±	12.30	30.19 ±	45.47
APOA1	393.39 ±	1310.33	1972.72 ±	4270.35
APOA2	23.61 ±	48.88	112.96 ±	177.26
APOA4	6.67 ±	27.91	40.48 ±	177.28
APOB	16.79 ±	34.39	125.98 ±	252.98
APOC1	1.09 ±	2.22	3.86 ±	6.09
APOC3	1.13 ±	2.15	3.60 ±	7.62
APOD	3.77 ±	9.09	18.15 ±	31.27
APOE	2.47 ±	4.03	9.47 ±	20.45
APOH	119.35 ±	123.59	628.23 ±	681.55
APOL1	9.09 ±	11.81	32.90 ±	53.86
C1 inactivator	16.53 ±	26.95	120.23 ±	168.84

CERU	139.29 ±	139.85	924.68 ±	1146.62
CFAH	51.37 ±	75.28	565.39 ±	768.37
CFB	50.62 ±	56.78	340.67 ±	429.09
CLUS	657.87 ±	710.96	1342.80 ±	1379.87
CO3	1531.55 ±	1535.86	7188.64 ±	7969.05
CO9	10.42 ±	14.09	59.54 ±	121.30
CRP	0.78 ±	1.16	17.32 ±	62.11
FA12	5.45 ±	10.02	35.34 ±	56.66
FETUA	40.13 ±	61.93	299.15 ±	370.60
FIBA	96.19 ±	324.46	679.58 ±	2360.06
FIBB	271.09 ±	339.35	2147.44 ±	2702.80
FIBG	0.41 ±	1.12	0.77 ±	2.52
FINC	101.67 ±	172.90	1169.04 ±	1807.32
FPA	89.63 ±	239.98	256.58 ±	772.60
GELS	1731.12 ±	2150.54	2712.18 ±	3070.35
HEMO	1186.39 ±	1548.09	6361.68 ±	6792.82
HEP2	10.60 ±	21.88	91.45 ±	138.77
HPT	6211.79 ±	8056.01	34774.55 ±	43027.34
HRG	74.06 ±	92.41	398.36 ±	514.63
ITIH1	58.79 ±	96.74	381.44 ±	646.21
KNG1	209.84 ±	292.61	1048.61 ±	1249.90
PLMN	4.71 ±	7.63	23.76 ±	30.87
Q9UJ43	5.36 ±	10.93	16.68 ±	22.37
RBP	149.04 ±	193.50	608.04 ±	846.12
SAA4	14.46 ±	31.18	85.68 ±	171.17
SAMP	2.35 ±	2.73	19.19 ±	18.79
THRB	0.90 ±	1.08	3.82 ±	8.60

TRFE	1621.78 ±	2013.46	7297.56 ±	9100.08
TSP1	240.83 ±	418.01	458.36 ±	647.83
TTHY	566.24 ±	783.77	1819.35 ±	2212.13
VTDB	252.48 ±	226.47	1138.24 ±	1253.76
VTNC	50.46 ±	106.88	392.89 ±	631.27
ZA2G	7927.88 ±	11941.30	7597.46 ±	7169.05

Supplemental Table S6. The results of differentiation of OSCC from control using cut-off concentrations defined by Youden's index and outlier analysis.

	Control vs. OSCC (n=58 vs. 61)								
				Youden's index			Outlier analysis		
Protein	fold-change	*p*-value	AUC value	Cut-off concentration [a] (ng/mL)	sensitivity	specificity	Cut-off concentration [b] (ng/mL)	sensitivity	specificity
A1AG1	2.42	0.001	0.67	32.31	0.49	0.84	127.01	0.11	0.97
A1AT	6.34	<0.001	0.87	213.04	0.87	0.79	4253.80	0.11	0.98
A1BG	4.48	<0.001	0.82	532.38	0.75	0.78	1572.46	0.36	1.00
A2AP	4.11	0.001	0.68	12.33	0.67	0.78	121.55	0.11	0.98
A2MG	3.83	<0.001	0.77	2912.78	0.79	0.67	21358.74	0.20	0.98
AACT	5.4	<0.001	0.75	29.44	0.64	0.76	403.83	0.20	0.97
ADIPO	3.79	<0.001	0.7	0.30	0.64	0.78	1.89	0.16	0.97
AFAM	3.94	<0.001	0.81	26.89	0.85	0.71	242.29	0.23	0.97
ALBU	3.92	<0.001	0.81	176368.09	0.69	0.79	540561.26	0.26	0.97
ANGT	5.03	<0.001	0.82	82.41	0.67	0.83	258.62	0.25	0.97
ANT3	6.28	<0.001	0.78	12.64	0.67	0.78	65.65	0.25	0.97
ANXA5	3.68	<0.001	0.7	13.15	0.57	0.86	49.07	0.15	0.97
APOA1	5.01	<0.001	0.73	301.46	0.62	0.84	4902.41	0.15	0.98

APOA2	4.79	<0.001	0.77	33.02	0.62	0.86	183.78	0.16	0.98
APOA4	6.07	0.001	0.67	0.18	0.67	0.66	101.80	0.08	0.97
APOB	7.5	<0.001	0.79	14.04	0.74	0.78	128.33	0.26	0.98
APOC1	3.52	<0.001	0.69	1.30	0.56	0.79	8.11	0.15	0.98
APOC3	3.19	0.081	0.59	1.10	0.41	0.79	7.42	0.13	0.97
APOD	4.82	0.002	0.65	16.62	0.36	0.95	31.57	0.16	0.98
APOE	3.83	0.001	0.67	1.98	0.61	0.72	14.81	0.15	0.97
APOH	5.26	<0.001	0.86	178.93	0.80	0.84	510.08	0.43	0.97
APOL1	3.62	<0.001	0.71	8.26	0.69	0.71	47.45	0.18	0.98
C1 inactivator	7.27	<0.001	0.83	36.73	0.64	0.91	120.35	0.28	0.97
CERU	6.64	<0.001	0.85	310.05	0.70	0.90	604.74	0.51	1.00
CFAH	11.01	<0.001	0.91	69.70	0.87	0.84	298.16	0.52	0.97
CFB	6.73	<0.001	0.85	93.75	0.75	0.83	230.10	0.43	0.98
CLUS	2.04	0.001	0.67	629.56	0.64	0.72	2806.87	0.13	0.97
CO3	4.69	<0.001	0.81	5967.30	0.39	1.00	6441.80	0.36	1.00
CO9	5.71	<0.001	0.7	14.64	0.57	0.79	56.06	0.25	0.98
CRP	22.19	<0.001	0.77	2.21	0.54	0.93	4.44	0.31	0.95
FA12	6.49	<0.001	0.83	6.24	0.79	0.74	37.06	0.25	0.98
FETUA	7.45	<0.001	0.85	86.51	0.70	0.90	239.78	0.41	0.95

FIBA	7.06	<0.001	0.74	14.17	0.75	0.71	1146.06	0.11	0.98
FIBB	7.92	<0.001	0.83	522.82	0.72	0.81	1325.80	0.49	1.00
FIBG	1.88	0.032	0.61	0.11	0.46	0.83	3.91	0.03	0.97
FINC	11.5	<0.001	0.84	137.81	0.79	0.81	668.13	0.48	0.98
FPA	2.86	0.803	0.49	148.17	0.20	0.93	870.70	0.08	0.97
GELS	1.57	0.013	0.63	589.06	0.90	0.40	8614.31	0.07	0.98
HEMO	5.36	<0.001	0.85	1607.47	0.75	0.81	6095.30	0.33	0.97
HEP2	8.63	<0.001	0.9	17.46	0.80	0.91	78.15	0.31	0.98
HPT	5.6	<0.001	0.79	6798.48	0.72	0.74	31306.97	0.36	0.98
HRG	5.38	<0.001	0.85	139.51	0.69	0.90	364.19	0.31	0.98
ITIH1	6.49	<0.001	0.85	87.01	0.75	0.83	372.65	0.26	0.98
KNG1	5	<0.001	0.83	289.63	0.74	0.79	1168.72	0.28	0.97
PLMN	5.04	<0.001	0.82	7.22	0.67	0.83	30.40	0.25	0.98
Q9UJ43	3.11	<0.001	0.71	7.42	0.56	0.84	40.55	0.13	0.97
RBP	4.08	<0.001	0.79	60.11	0.95	0.48	757.53	0.25	0.98
SAA4	5.92	<0.001	0.76	13.03	0.64	0.79	118.95	0.21	0.97
SAMP	8.16	<0.001	0.88	5.21	0.77	0.90	11.16	0.54	0.97
THRB	4.24	<0.001	0.71	1.22	0.61	0.78	4.20	0.23	0.98
TRFE	4.5	<0.001	0.8	2580.88	0.70	0.84	7873.46	0.26	0.98
TSP1	1.9	0.004	0.65	197.52	0.61	0.74	1499.26	0.05	0.98

TTHY	3.21	<0.001	0.74	842.30	0.52	0.86	3248.27	0.20	0.98
VTDB	4.51	<0.001	0.87	303.68	0.82	0.78	951.37	0.38	1.00
VTNC	7.79	<0.001	0.87	108.38	0.72	0.91	397.00	0.26	0.98
ZA2G	0.96	0.102	0.59	1699.95	0.85	0.40	43538.45	0.00	0.97

[a] : The optimal cutoff point is determined using Youden's index (*J*), calculated as *J* = 1 – (false positive rate + false negative rate) = 1 – [(1 – sensitivity) + (1 – specificity)] = sensitivity + specificity – 1.

[b] : The outlier-cutoff value is defined using control specimens by outlier analysis based on T_n-test, and is determined as the closest concentration in the ROC curve for presentation of sensitivity/specificity values. Generally, the specificity at outlier-cutoff point is very high, therefore, the sensitivity is lower than the one of Youden's index.

Supplemental Table S7. Multivariate Logistic Regression Analysis

	Adjusted Odds Ratio	95% Confidence Interval	P
AFAM	0.949	0.919 ～ 0.980	0.002
CFAH	1.024	1.008 ～ 1.041	0.003
GELS	0.998	0.997 ～ 0.999	0.000
SAMP	1.444	1.095 ～ 1.904	0.009
VTDB	1.012	1.005 ～ 1.020	0.002

Supplemental references

(1) Boichenko, A. P.; Govorukhina, N.; Klip, H. G.; van der Zee, A. G.; Guzel, C.; Luider, T. M.; Bischoff, R. *Journal of proteome research* **2014**, *13*, 4995-5007.

(2) Chirwa, N.; Govender, D.; Ndimba, B.; Lotz, Z.; Tyler, M.; Panieri, E.; Kahn, D.; Mall, A. S. *Journal of Cancer* **2012**, *3*, 83-92.

(3) Semaan, S. M.; Wang, X.; Marshall, A. G.; Sang, Q. X. *Journal of Cancer* **2012**, *3*, 269-284.

(4) Liu, Y.; Luo, X.; Hu, H.; Wang, R.; Sun, Y.; Zeng, R.; Chen, H. *PloS one* **2012**, *7*, e51748.

(5) Reed, G. L.; Houng, A. K.; Wang, D. *Arteriosclerosis, thrombosis, and vascular biology* **2014**, *34*, 2586-2593.

(6) Chen, Y. T.; Chen, H. W.; Domanski, D.; Smith, D. S.; Liang, K. H.; Wu, C. C.; Chen, C. L.; Chung, T.; Chen, M. C.; Chang, Y. S.; Parker, C. E.; Borchers, C. H.; Yu, J. S. *J. Proteomics* **2012**, *75*, 3529-3545.

(7) Poon, T. C.; Chan, A. T.; Zee, B.; Ho, S. K.; Mok, T. S.; Leung, T. W.; Johnson, P. J. *Oncology* **2001**, *61*, 275-283.

(8) Nie, S.; Lo, A.; Wu, J.; Zhu, J.; Tan, Z.; Simeone, D. M.; Anderson, M. A.; Shedden, K. A.; Ruffin, M. T.; Lubman, D. M. *Journal of proteome research* **2014**, *13*, 1873-1884.

(9) Nie, S.; Yin, H.; Tan, Z.; Anderson, M. A.; Ruffin, M. T.; Simeone, D. M.; Lubman, D. M. *J. Proteome Res.* **2014**, *13*, 6058-6066.

(10) Zeng, F.; Shi, J.; Long, Y.; Tian, H.; Li, X.; Zhao, A. Z.; Li, R. F.; Chen, T. *Cellular physiology and biochemistry : international journal of experimental cellular physiology, biochemistry, and pharmacology* **2015**, *36*, 1670-1678.

(11) Seeber, B.; Morandell, E.; Lunger, F.; Wildt, L.; Dieplinger, H. *Reproductive biology and endocrinology : RB&E* **2014**, *12*, 88.

(12) Song, H. J.; Xue, Y. L.; Qiu, Z. L.; Luo, Q. Y. *Nuclear medicine communications* **2013**, *34*, 1196-1203.

(13) Aktas, B.; Kasimir-Bauer, S.; Wimberger, P.; Kimmig, R.; Heubner, M. *Anticancer research* **2013**, *33*, 329-336.

(14) Shibutani, M.; Maeda, K.; Nagahara, H.; Ohtani, H.; Iseki, Y.; Ikeya, T.; Sugano, K.; Hirakawa, K. *BMC cancer* **2015**, *15*, 521.

(15) Zhou, T.; Zhan, J.; Hong, S.; Hu, Z.; Fang, W.; Qin, T.; Ma, Y.; Yang, Y.; He, X.; Zhao, Y.; Huang, Y.; Zhao, H.; Zhang, L. *Scientific reports* **2015**, *5*, 10481.

(16) Martin, P.; Noonan, S.; Mullen, M. P.; Scaife, C.; Tosetto, M.; Nolan, B.; Wynne, K.; Hyland, J.; Sheahan, K.; Elia, G.; O'Donoghue, D.; Fennelly, D.; O'Sullivan, J. *BMC cancer* **2014**, *14*, 887.

(17) Luo, Y.; Ohmori, H.; Shimomoto, T.; Fujii, K.; Sasahira, T.; Chihara, Y.; Kuniyasu, H. *Pathobiology : journal of immunopathology, molecular and cellular biology* **2011**, *78*, 285-290.

(18) Iwako, H.; Tashiro, H.; Amano, H.; Tanimoto, Y.; Oshita, A.; Kobayashi, T.; Kuroda, S.; Tazawa, H.; Nambu, J.; Mikuriya, Y.; Abe, T.; Ohdan, H. *Ann. Surg. Oncol.* **2012**, *19*, 2888-2896.

(19) Kuusisto, M. E.; Haapasaari, K. M.; Remes, A. M.; Bloigu, R.; Karihtala, P.; Turpeenniemi-Hujanen, T.; Kuittinen, O. *Ann. Hematol.* **2015**, *94*, 1167-1174.

(20) Park, N.; Chun, Y. J. *Journal of toxicology and environmental health. Part A* **2014**, *77*, 1467-1476.

(21) Wu, L.; Yang, L.; Xiong, Y.; Guo, H.; Shen, X.; Cheng, Z.; Zhang, Y.; Gao, Z.; Zhu, X. *Tumour biology : the journal of the International Society for Oncodevelopmental Biology and Medicine* **2014**, *35*, 12327-12337.

(22) Chen, Y. T.; Chen, C. L.; Chen, H. W.; Chung, T.; Wu, C. C.; Chen, C. D.; Hsu, C. W.; Chen, M. C.; Tsui, K. H.; Chang, P. L.; Chang, Y. S.; Yu, J. S. *J. Proteome Res.* **2010**, *9*, 5803-5815.

(23) Pal, M. K.; Rashid, M.; Bisht, M. *Biosensors & bioelectronics* **2015**, *73*, 146-152.

(24) Soukup, V.; Kalousova, M.; Capoun, O.; Sobotka, R.; Breyl, Z.; Pesl, M.; Zima, T.; Hanus, T. *Urologia*

internationalis **2015**.
(25) Huang, Y.; Zhang, X.; Jiang, W.; Wang, Y.; Jin, H.; Liu, X.; Xu, C. *European journal of obstetrics, gynecology, and reproductive biology* **2012**, *165*, 96-103.
(26) Guo, X.; Hao, Y.; Kamilijiang, M.; Hasimu, A.; Yuan, J.; Wu, G.; Reyimu, H.; Kadeer, N.; Abudula, A. *Tumour biology : the journal of the International Society for Oncodevelopmental Biology and Medicine* **2015**, *36*, 1711-1720.
(27) Timms, J. F.; Arslan-Low, E.; Kabir, M.; Worthington, J.; Camuzeaux, S.; Sinclair, J.; Szaub, J.; Afrough, B.; Podust, V. N.; Fourkala, E. O.; Cubizolles, M.; Kronenberg, F.; Fung, E. T.; Gentry-Maharaj, A.; Menon, U.; Jacobs, I. *Proteomics. Clinical applications* **2014**, *8*, 982-993.
(28) Chen, C. L.; Lin, T. S.; Tsai, C. H.; Wu, C. C.; Chung, T.; Chien, K. Y.; Wu, M.; Chang, Y. S.; Yu, J. S.; Chen, Y. T. *Journal of proteomics* **2013**, *85*, 28-43.
(29) Gong, Y.; Zhang, L.; Bie, P.; Wang, H. *PloS one* **2013**, *8*, e61456.
(30) Zhang, X.; Zhao, X. W.; Liu, D. B.; Han, C. Z.; Du, L. L.; Jing, J. X.; Wang, Y. *World journal of gastroenterology : WJG* **2014**, *20*, 8646-8652.
(31) Fukuhara, T.; Wada, M.; Nakamura, S.; Ono, C.; Shiokawa, M.; Yamamoto, S.; Motomura, T.; Okamoto, T.; Okuzaki, D.; Yamamoto, M.; Saito, I.; Wakita, T.; Koike, K.; Matsuura, Y. *PLoS pathogens* **2014**, *10*, e1004534.
(32) Cohen, M.; Yossef, R.; Erez, T.; Kugel, A.; Welt, M.; Karpasas, M. M.; Bones, J.; Rudd, P. M.; Taieb, J.; Boissin, H.; Harats, D.; Noy, K.; Tekoah, Y.; Lichtenstein, R. G.; Rubin, E.; Porgador, A. *PloS one* **2011**, *6*, e14540.
(33) Bajo-Graneras, R.; Crespo-Sanjuan, J.; Garcia-Centeno, R. M.; Garrote-Adrados, J. A.; Gutierrez, G.; Garcia-Tejeiro, M.; Aguirre-Gervas, B.; Calvo-Nieves, M. D.; Bustamante, R.; Ganfornina, M. D.; Sanchez, D. *International journal of colorectal disease* **2013**, *28*, 751-766.
(34) Soiland, H.; Skaland, I.; Varhaug, J. E.; Korner, H.; Janssen, E. A.; Gudlaugsson, E.; Baak, J. P.; Soreide, J. A. *Acta oncologica* **2009**, *48*, 514-521.
(35) Chung, L.; Moore, K.; Phillips, L.; Boyle, F. M.; Marsh, D. J.; Baxter, R. C. *Breast cancer research : BCR* **2014**, *16*, R63.
(36) Pietrowska, M.; Jelonek, K.; Michalak, M.; Ros, M.; Rodziewicz, P.; Chmielewska, K.; Polanski, K.; Polanska, J.; Gdowicz-Klosok, A.; Giglok, M.; Suwinski, R.; Tarnawski, R.; Dziadziuszko, R.; Rzyman, W.; Widlak, P. *Acta biochimica Polonica* **2014**, *61*, 325-331.
(37) Dummer, P. D.; Limou, S.; Rosenberg, A. Z.; Heymann, J.; Nelson, G.; Winkler, C. A.; Kopp, J. B. *Seminars in nephrology* **2015**, *35*, 222-236.
(38) Limou, S.; Nelson, G. W.; Lecordier, L.; An, P.; O'HUigin, C. S.; David, V. A.; Binns-Roemer, E. A.; Guiblet, W. M.; Oleksyk, T. K.; Pays, E.; Kopp, J. B.; Winkler, C. A. *Kidney international* **2015**.
(39) Hu, C. A.; Klopfer, E. I.; Ray, P. E. *FEBS letters* **2012**, *586*, 947-955.
(40) Monnier, N.; Ponard, D.; Duponchel, C.; Csopaki, F.; Bouillet, L.; Tosi, M.; Lunardi, J.; Drouet, C. *Molecular immunology* **2006**, *43*, 2161-2168.
(41) Caballero, T.; Farkas, H.; Bouillet, L.; Bowen, T.; Gompel, A.; Fagerberg, C.; Bjokander, J.; Bork, K.; Bygum, A.; Cicardi, M.; de Carolis, C.; Frank, M.; Gooi, J. H.; Longhurst, H.; Martinez-Saguer, I.; Nielsen, E. W.; Obtulowitz, K.; Perricone, R.; Prior, N.; Group, C. I. D. W. *The Journal of allergy and clinical immunology* **2012**, *129*, 308-320.
(42) Diaconu, C.; Pantis, C.; Cirimbei, C.; Bordea, C.; Gruia, M. I.; Blidaru, A. *Journal of medicine and life* **2015**, *8*, 32-36.
(43) Balmana, M.; Sarrats, A.; Llop, E.; Barrabes, S.; Saldova, R.; Ferri, M. J.; Figueras, J.; Fort, E.; de Llorens, R.; Rudd, P. M.; Peracaula, R. *Clinica chimica acta; international journal of clinical chemistry* **2015**, *442*, 56-62.

(44) Benicky, J.; Sanda, M.; Pompach, P.; Wu, J.; Goldman, R. *Analytical chemistry* **2014**, *86*, 10716-10723.
(45) Riihila, P. M.; Nissinen, L. M.; Ala-aho, R.; Kallajoki, M.; Grenman, R.; Meri, S.; Peltonen, S.; Peltonen, J.; Kahari, V. M. *The Journal of investigative dermatology* **2014**, *134*, 498-506.
(46) Wu, J.; Xie, X.; Nie, S.; Buckanovich, R. J.; Lubman, D. M. *Journal of proteome research* **2013**, *12*, 3342-3352.
(47) Lee, M. J.; Na, K.; Jeong, S. K.; Lim, J. S.; Kim, S. A.; Lee, M. J.; Song, S. Y.; Kim, H.; Hancock, W. S.; Paik, Y. K. *Journal of proteome research* **2014**, *13*, 4878-4888.
(48) Seriramalu, R.; Pang, W. W.; Jayapalan, J. J.; Mohamed, E.; Abdul-Rahman, P. S.; Bustam, A. Z.; Khoo, A. S.; Hashim, O. H. *Electrophoresis* **2010**, *31*, 2388-2395.
(49) Xiu, P.; Dong, X. F.; Li, X. P.; Li, J. *World journal of gastroenterology : WJG* **2015**, *21*, 8262-8270.
(50) Guo, W.; Ma, X.; Xue, C.; Luo, J.; Zhu, X.; Xiang, J.; Lu, B.; Li, H. *Disease markers* **2014**, *2014*, 168960.
(51) Paulus, Y. M.; Kuo, C. H.; Morohoshi, K.; Nugent, A.; Zheng, L. L.; Nomoto, H.; Blumenkranz, M. S.; Palanker, D.; Ono, S. J. *Ophthalmic surgery, lasers & imaging retina* **2015**, *46*, 362-368.
(52) Kim, P. Y.; Tan, O.; Diakiw, S. M.; Carter, D.; Sekerye, E. O.; Wasinger, V. C.; Liu, T.; Kavallaris, M.; Norris, M. D.; Haber, M.; Chesler, L.; Dolnikov, A.; Trahair, T. N.; Cheung, N. K.; Marshall, G. M.; Cheung, B. B. *Journal of proteomics* **2014**, *96*, 1-12.
(53) Narayanasamy, A.; Ahn, J. M.; Sung, H. J.; Kong, D. H.; Ha, K. S.; Lee, S. Y.; Cho, J. Y. *Journal of proteomics* **2011**, *74*, 2948-2958.
(54) Fan, N. J.; Kang, R.; Ge, X. Y.; Li, M.; Liu, Y.; Chen, H. M.; Gao, C. F. *Diagnostic pathology* **2014**, *9*, 53.
(55) Linden, M.; Lind, S. B.; Mayrhofer, C.; Segersten, U.; Wester, K.; Lyutvinskiy, Y.; Zubarev, R.; Malmstrom, P. U.; Pettersson, U. *Proteomics* **2012**, *12*, 135-144.
(56) Tung, C. L.; Lin, S. T.; Chou, H. C.; Chen, Y. W.; Lin, H. C.; Tung, C. L.; Huang, K. J.; Chen, Y. J.; Lee, Y. R.; Chan, H. L. *Journal of pharmaceutical and biomedical analysis* **2013**, *75*, 7-17.
(57) Zhou, Z.; Qutaish, M.; Han, Z.; Schur, R. M.; Liu, Y.; Wilson, D. L.; Lu, Z. R. *Nature communications* **2015**, *6*, 7984.
(58) Ebert, M. P.; Niemeyer, D.; Deininger, S. O.; Wex, T.; Knippig, C.; Hoffmann, J.; Sauer, J.; Albrecht, W.; Malfertheiner, P.; Rocken, C. *Journal of proteome research* **2006**, *5*, 2152-2158.
(59) Xin, Y. N.; Geng, N.; Lin, Z. H.; Cui, Y. Z.; Duan, H. P.; Zhang, M.; Xuan, S. Y. *PloS one* **2014**, *9*, e108132.
(60) Lokamani, I.; Looi, M. L.; Md Ali, S. A.; Mohd Dali, A. Z.; Ahmad Annuar, M. A.; Jamal, R. *Pathology oncology research : POR* **2014**, *20*, 119-129.
(61) Pan, T. L.; Wang, P. W.; Al-Suwayeh, S. A.; Huang, Y. J.; Fang, J. Y. *Food and chemical toxicology : an international journal published for the British Industrial Biological Research Association* **2012**, *50*, 3892-3901.
(62) Kalantari, S.; Rutishauser, D.; Samavat, S.; Nafar, M.; Mahmudieh, L.; Rezaei-Tavirani, M.; Zubarev, R. A. *PloS one* **2013**, *8*, e80830.
(63) Jessie, K.; Jayapalan, J. J.; Ong, K. C.; Abdul Rahim, Z. H.; Zain, R. M.; Wong, K. T.; Hashim, O. H. *Electrophoresis* **2013**, *34*, 2495-2502.
(64) Clarke, L. A.; Hemmelgarn, H.; Colobong, K.; Thomas, A.; Stockler, S.; Casey, R.; Chan, A.; Fernoff, P.; Mitchell, J. *Journal of inherited metabolic disease* **2012**, *35*, 355-362.
(65) Ayyub, A.; Saleem, M.; Musharraf, S. G.; Naz, M.; Tariq, A.; Hashmi, N. *Molecular medicine reports* **2015**, *12*, 3755-3762.
(66) Matboli, M.; Eissa, S.; Said, H. *Medical oncology* **2014**, *31*, 897.
(67) Qiu, Y.; Patwa, T. H.; Xu, L.; Shedden, K.; Misek, D. E.; Tuck, M.; Jin, G.; Ruffin, M. T.; Turgeon, D. K.; Synal, S.; Bresalier, R.; Marcon, N.; Brenner, D. E.; Lubman, D. M. *Journal of proteome research* **2008**, *7*, 1693-1703.
(68) Halder, S.; Dey, R. K.; Chowdhury, A. R.; Bhattacharyya, P.; Chakrabarti, A. *Journal of proteomics* **2015**.

(69) Wang, J.; Wang, X.; Lin, S.; Chen, C.; Wang, C.; Ma, Q.; Jiang, B. *PloS one* **2013**, *8*, e70519.
(70) Liu, W.; Liu, B.; Cai, Q.; Li, J.; Chen, X.; Zhu, Z. *Clinica chimica acta; international journal of clinical chemistry* **2012**, *413*, 1098-1106.
(71) Didiasova, M.; Wujak, L.; Wygrecka, M.; Zakrzewicz, D. *International journal of molecular sciences* **2014**, *15*, 21229-21252.
(72) Liu, W.; Yang, Q.; Liu, B.; Zhu, Z. *Clinica chimica acta; international journal of clinical chemistry* **2014**, *431*, 179-184.
(73) Choudhary, D.; Hegde, P.; Voznesensky, O.; Choudhary, S.; Kopsiaftis, S.; Claffey, K. P.; Pilbeam, C. C.; Taylor, J. A., 3rd. *Urologic oncology* **2015**, *33*, 387 e317-327.
(74) Alkharfy, K. M.; Al-Daghri, N. M.; Vanhoutte, P. M.; Krishnaswamy, S.; Xu, A. *PloS one* **2012**, *7*, e48612.
(75) Cheng, Y.; Liu, C.; Zhang, N.; Wang, S.; Zhang, Z. *BioMed research international* **2014**, *2014*, 179040.
(76) Urieli-Shoval, S.; Finci-Yeheskel, Z.; Dishon, S.; Galinsky, D.; Linke, R. P.; Ariel, I.; Levin, M.; Ben-Shachar, I.; Prus, D. *The journal of histochemistry and cytochemistry : official journal of the Histochemistry Society* **2010**, *58*, 1015-1023.
(77) Cubedo, J.; Padro, T.; Badimon, L. *International journal of cardiology* **2013**, *168*, 5196-5204.
(78) Lech, M.; Rommele, C.; Anders, H. J. *Nephrology, dialysis, transplantation : official publication of the European Dialysis and Transplant Association - European Renal Association* **2013**, *28*, 803-811.
(79) Li, C.; Zang, T.; Wrobel, K.; Huang, J. T.; Nabi, G. *Analytical and bioanalytical chemistry* **2015**, *407*, 3393-3404.
(80) Song, P.; Feng, X.; Inagaki, Y.; Song, T.; Zhang, K.; Wang, Z.; Zheng, S.; Ma, K.; Li, Q.; Kong, D.; Wu, Q.; Zhang, T.; Zhao, X.; Hasegawa, K.; Sugawara, Y.; Kokudo, N.; Tang, W.; Japan-China Joint Team for Medical, R.; Cooperation on, H. C. C. *Bioscience trends* **2014**, *8*, 266-273.
(81) Bourseau-Guilmain, E.; Griveau, A.; Benoit, J. P.; Garcion, E. *PloS one* **2011**, *6*, e25515.
(82) Hogdall, C.; Fung, E. T.; Christensen, I. J.; Nedergaard, L.; Engelholm, S. A.; Petri, A. L.; Risum, S.; Lundvall, L.; Yip, C.; Pedersen, A. T.; Hartwell, D.; Lomas, L.; Hogdall, E. V. *Gynecologic oncology* **2011**, *123*, 308-313.
(83) Fleitas, T.; Martinez-Sales, V.; Vila, V.; Reganon, E.; Mesado, D.; Martin, M.; Gomez-Codina, J.; Montalar, J.; Reynes, G. *Clinical & translational oncology : official publication of the Federation of Spanish Oncology Societies and of the National Cancer Institute of Mexico* **2013**, *15*, 897-902.
(84) Ding, H.; Liu, J.; Xue, R.; Zhao, P.; Qin, Y.; Zheng, F.; Sun, X. *Biomedical reports* **2014**, *2*, 765-769.
(85) Chen, J.; Chen, L. J.; Xia, Y. L.; Zhou, H. C.; Yang, R. B.; Wu, W.; Lu, Y.; Hu, L. W.; Zhao, Y. *Journal of cancer research and clinical oncology* **2013**, *139*, 1117-1127.
(86) Carduner, L.; Agniel, R.; Kellouche, S.; Picot, C. R.; Blanc-Fournier, C.; Leroy-Dudal, J.; Carreiras, F. *Biochimica et biophysica acta* **2013**, *1830*, 4885-4897.
(87) Ahn, H. S.; Shin, Y. S.; Park, P. J.; Kang, K. N.; Kim, Y.; Lee, H. J.; Yang, H. K.; Kim, C. W. *British journal of cancer* **2012**, *106*, 733-739.
(88) Xue, Y.; Yu, F.; Yan, D.; Cui, F.; Tang, H.; Wang, X.; Chen, J.; Lu, H.; Zhao, S.; Peng, Z. *International journal of molecular sciences* **2015**, *16*, 691-703.
(89) Katafigiotis, I.; Tyritzis, S. I.; Stravodimos, K. G.; Alamanis, C.; Pavlakis, K.; Vlahou, A.; Makridakis, M.; Katafigioti, A.; Garbis, S. D.; Constantinides, C. A. *BJU international* **2012**, *110*, E688-693.
(90) Lim, S. C.; Liying, D. Q.; Toy, W. C.; Wong, M.; Yeoh, L. Y.; Tan, C.; Lau, D.; Tan, C.; Subramaniam, T.; Sum, C. F. *Diabetic medicine : a journal of the British Diabetic Association* **2012**, *29*, 945-949.