Fig. 1A

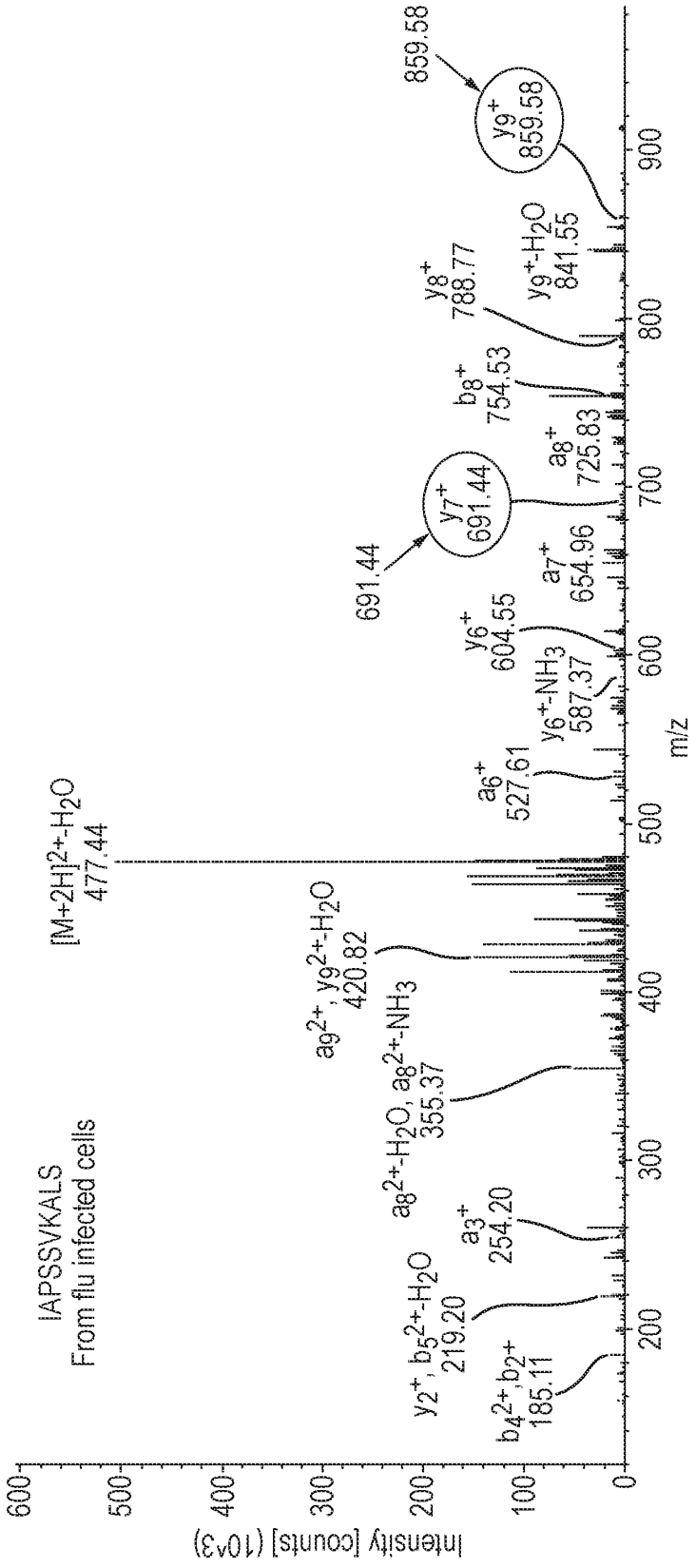

IAPSSVKALS
From flu infected cells
[M+2H]2+-H2O
477.44
ag2+, yg2+-H2O
420.82
ag2+-H2O, ag2+-NH3
355.37
a3+
254.20
y2+, b52+-H2O
219.20
b42+, b2+
185.11
a6+
527.61
y6+-NH3
587.37
y6+
604.55
691.44
y7+
691.44
a7+
654.96
a8+
725.83
b8+
754.53
y8+
788.77
y9+-H2O
841.55
859.58
y9+
859.58
Intensity [counts] (10^3)
m/z

Fig. 1B

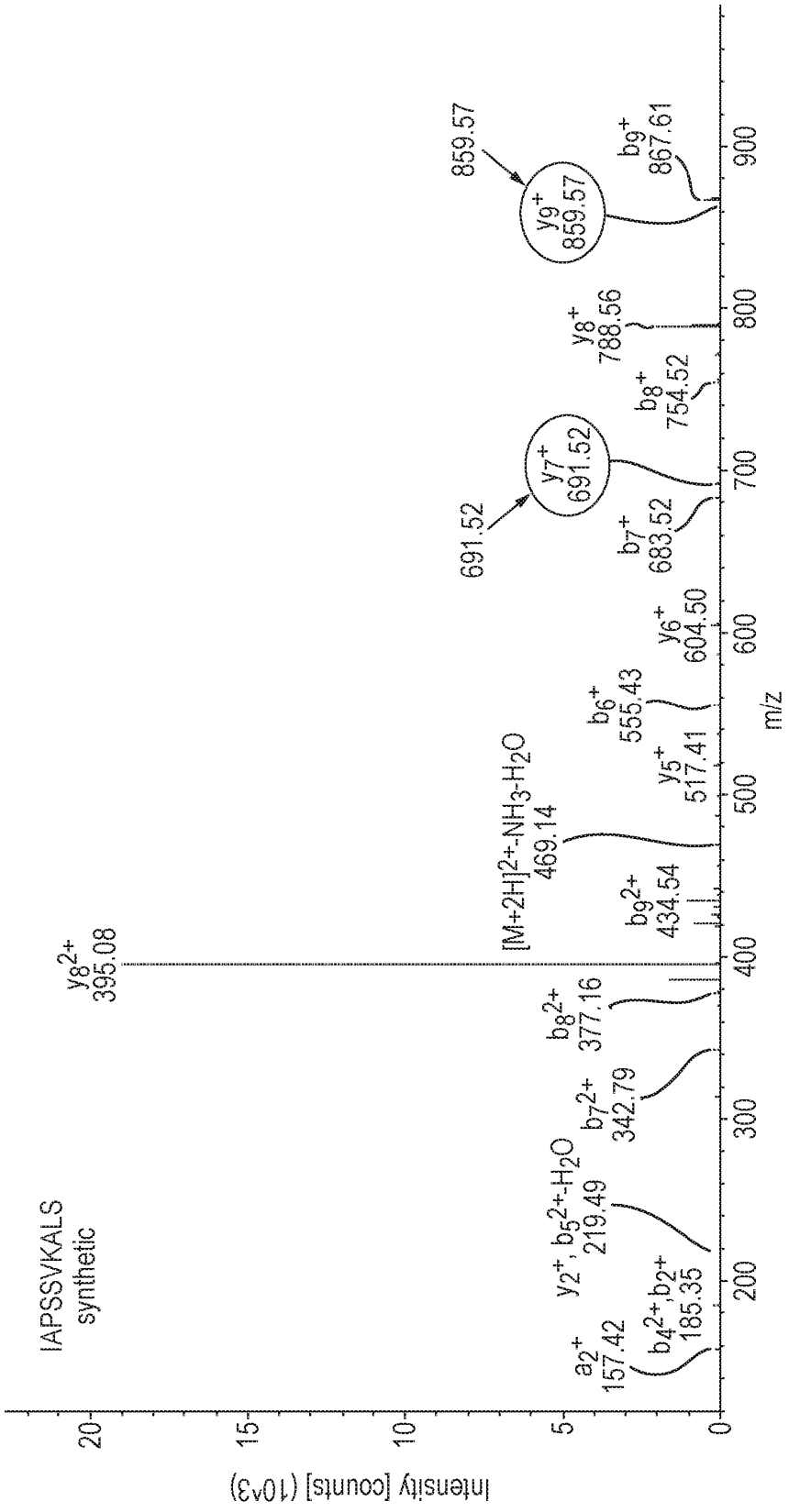

IAPSSVKALS
synthetic
Intensity [counts] (10^3)
m/z
y8 2+ 395.08
[M+2H]2+-NH3-H2O 469.14
b9 2+ 434.54
y5+ 517.41
b6+ 555.43
y6+ 604.50
691.52
y7+ 691.52
b7+ 683.52
b8+ 754.52
y8+ 788.56
859.57
y9+ 859.57
b9+ 867.61
b8 2+ 377.16
b7 2+ 342.79
y2+, b5 2+-H2O 219.49
b4 2+, b2+ 185.35
a2+ 157.42

Fig. 2A

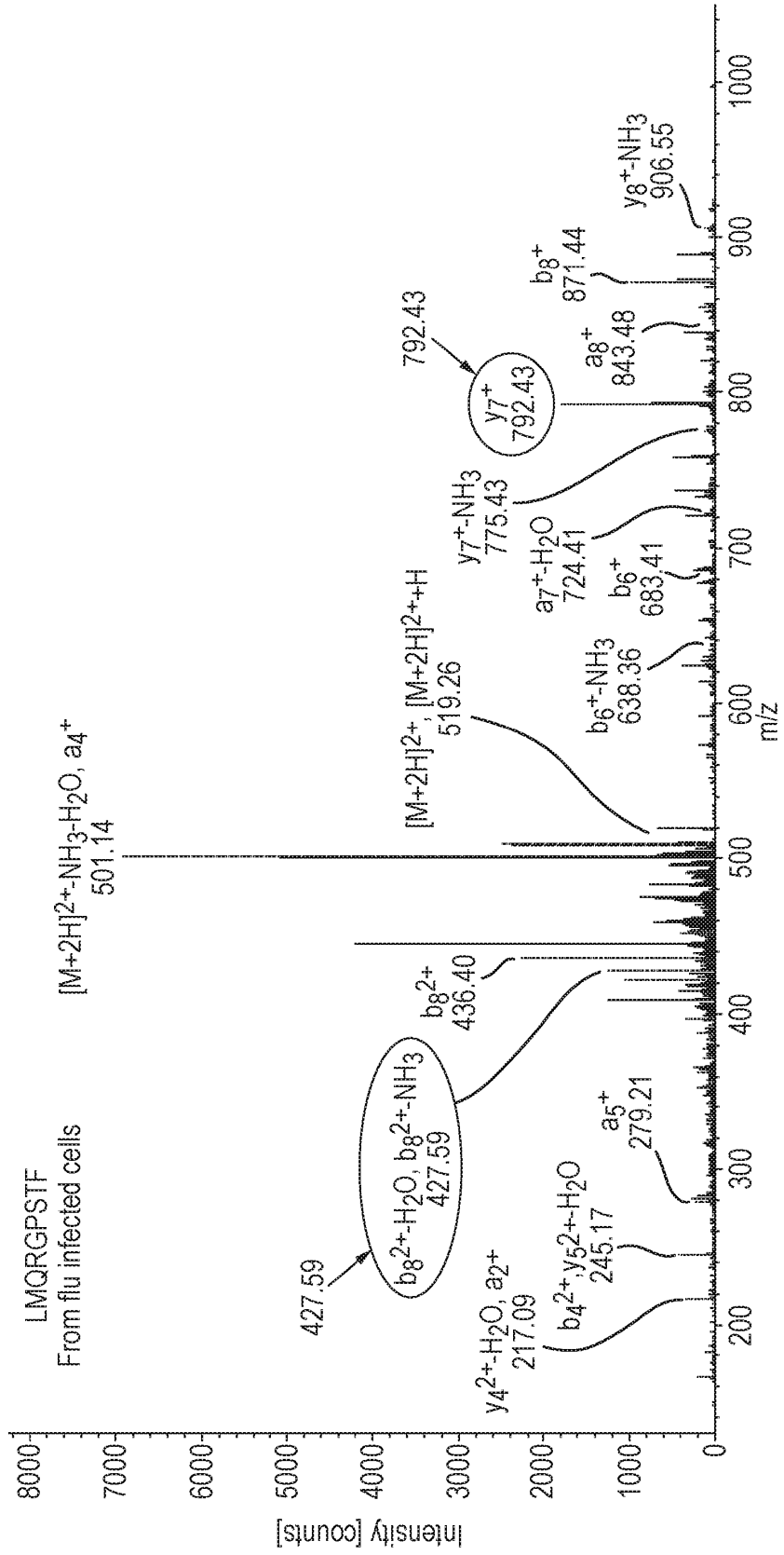

LMQRGPSTF
From flu infected cells
[M+2H]2+-NH3-H2O, a4+
501.14
[M+2H]2+, [M+2H]2+-H
519.26
792.43
y7+
792.43
b8+
871.44
y8+-NH3
906.55
a8+
843.48
y7+-NH3
775.43
a7+-H2O
724.41
b6+
683.41
b6+-NH3
638.36
b82+
436.40
427.59
b82+-H2O, b82+-NH3
427.59
a5+
279.21
b42+,y52+-H2O
245.17
y42+-H2O, a22+
217.09
Intensity [counts]
m/z

Fig. 2B

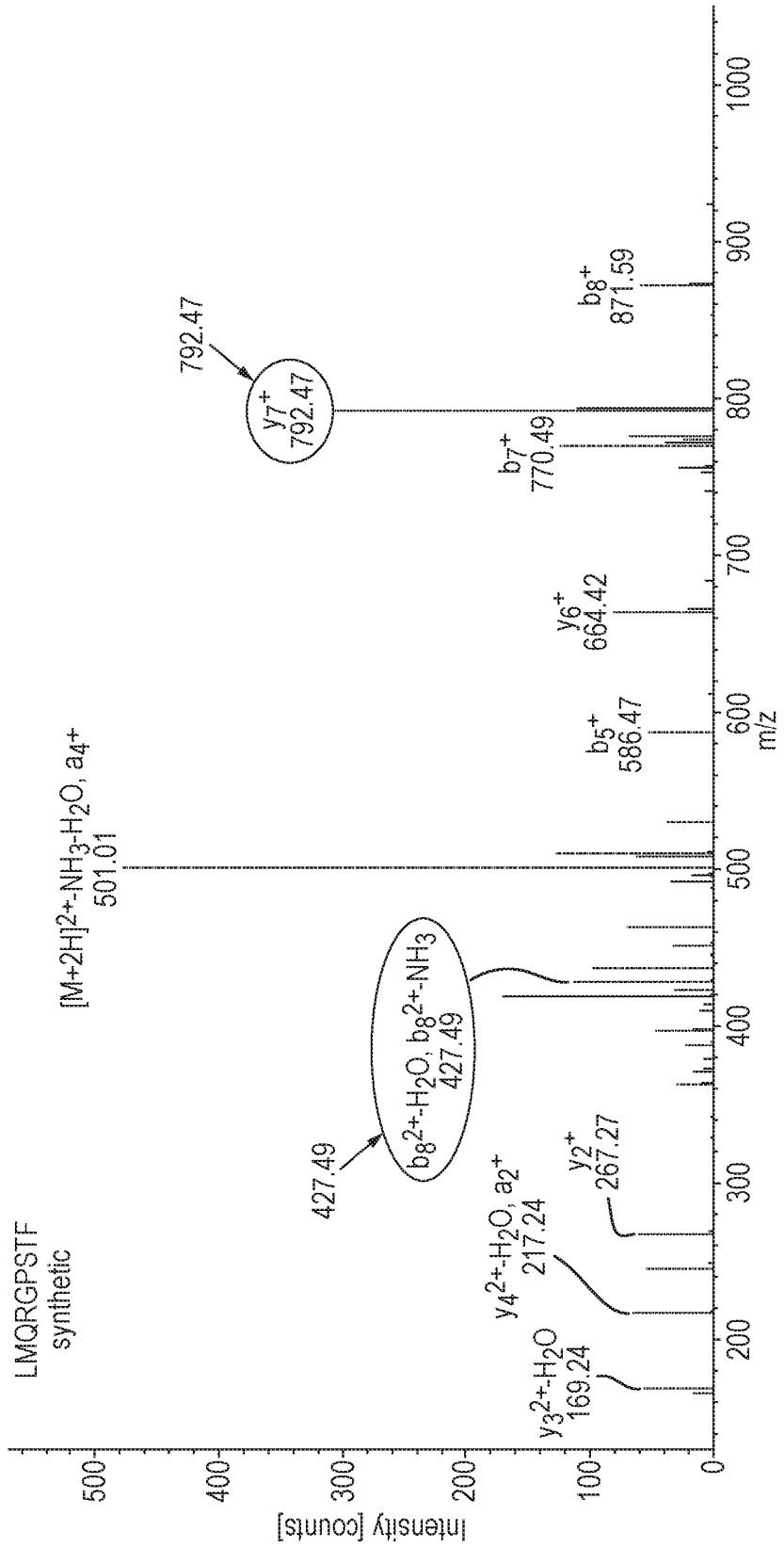

LMQRGPSTF
synthetic
[M+2H]2+-NH3-H2O, a4+
501.01
427.49
b82+-H2O, b82+-NH3
427.49
792.47
y7+
792.47
y42+-H2O, a2+
217.24
y32+-H2O
169.24
y2+
267.27
b7+
770.49
b8+
871.59
y6+
664.42
b5+
586.47
Intensity [counts]
m/z
0
100
200
300
400
500
200
300
400
500
600
700
800
900
1000

Fig. 3A

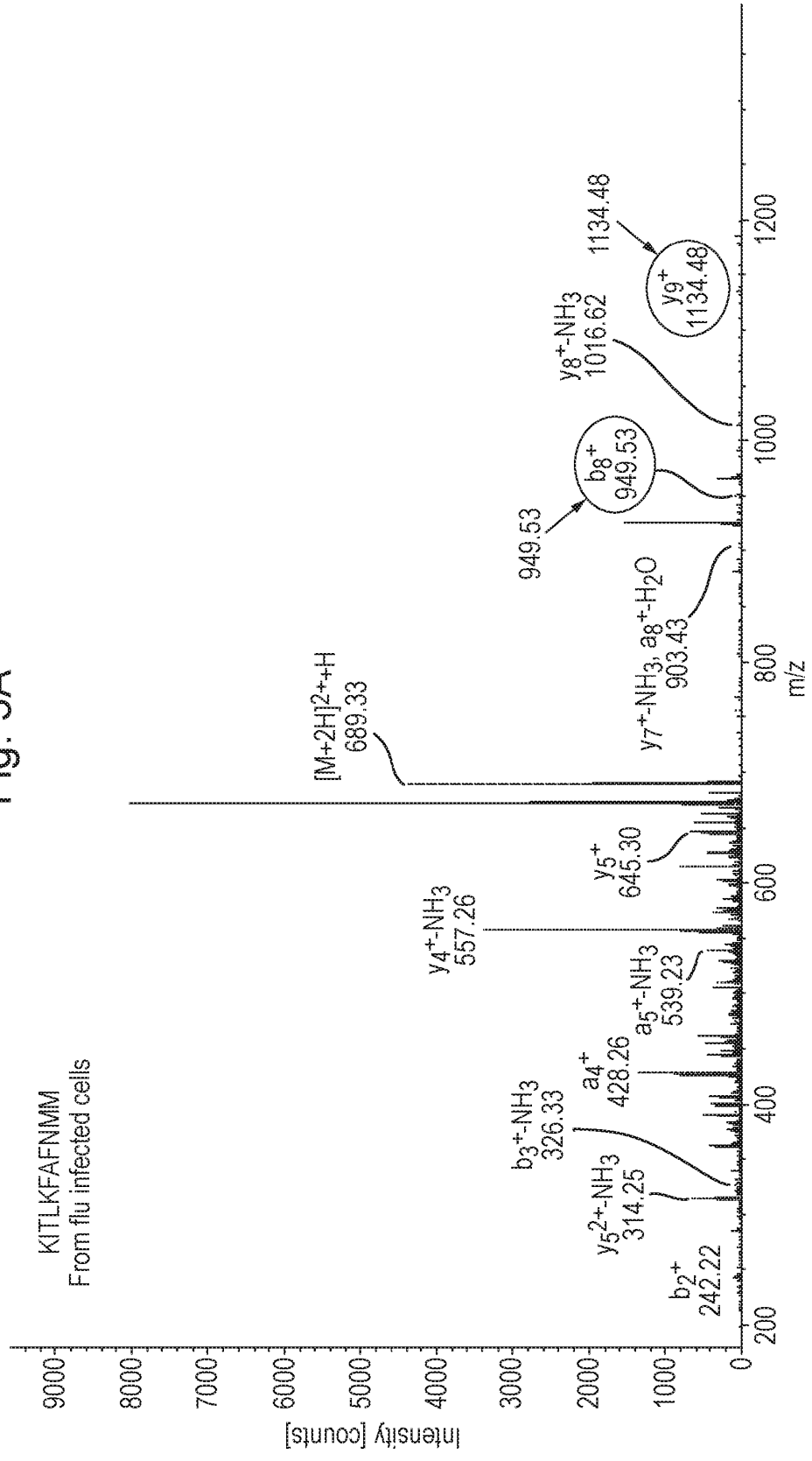

KITLKFAFNMM
From flu infected cells
Intensity [counts]
m/z
[M+2H]2+-H 689.33
949.53
b8+ 949.53
y8+-NH3 1016.62
1134.48
y9+ 1134.48
y7+-NH3, a8+-H2O 903.43
y4+-NH3 557.26
y5+ 645.30
b3+-NH3 326.33
a4+ 428.26
a5+-NH3 539.23
y52+-NH3 314.25
b2+ 242.22

Fig. 3B

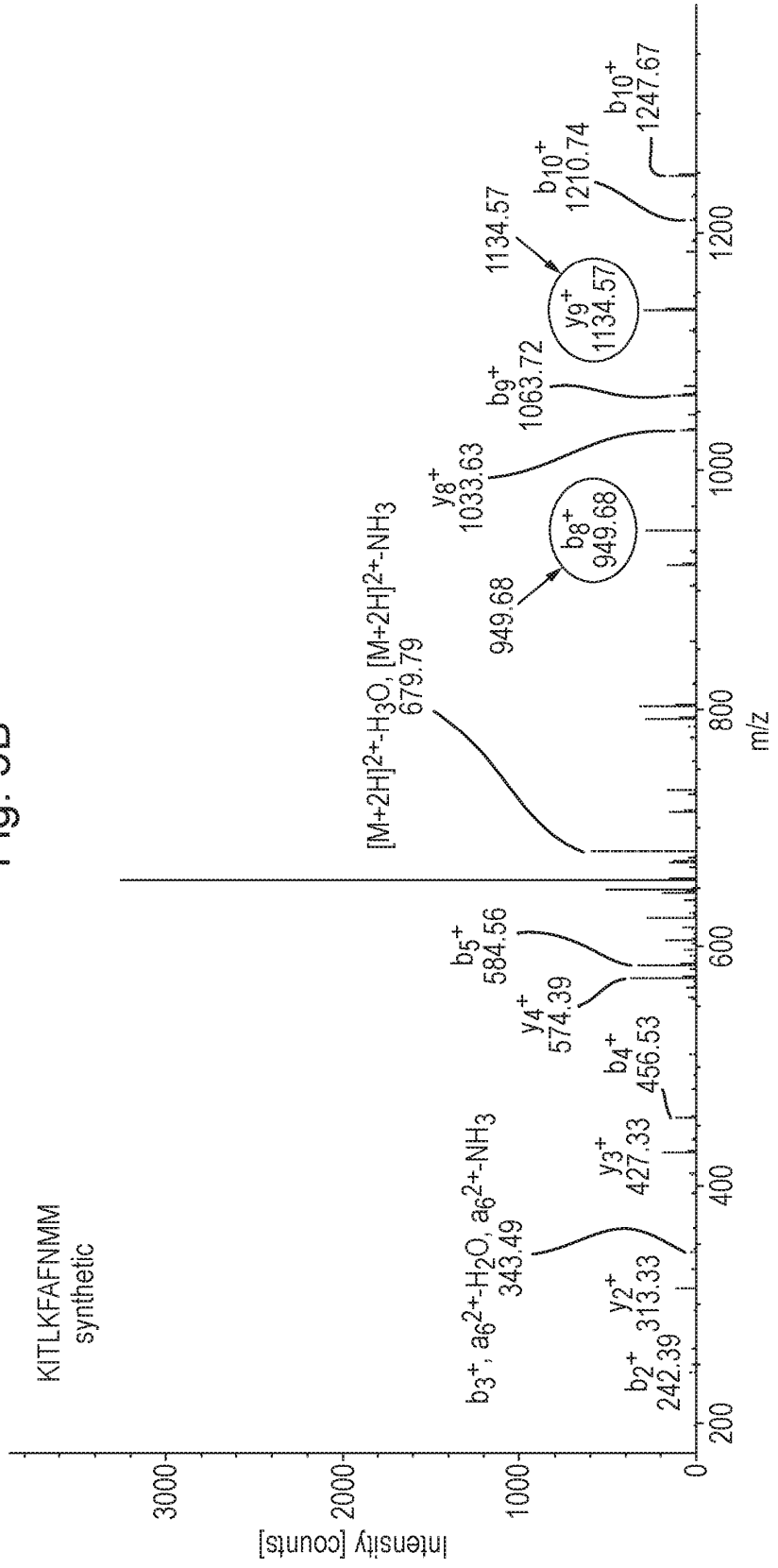

KITLKFAFNMM
synthetic
Intensity [counts]
m/z
[M+2H]2+-H3O, [M+2H]2+-NH3
679.79
949.68
b8+
949.68
y8+
1033.63
bg+
1063.72
1134.57
y9+
1134.57
b10+
1210.74
b10+
1247.67
b5+
584.56
y4+
574.39
b4+
456.53
y3+
427.33
y2+
313.33
b2+
242.39
b3+; a62+-H2O, a62+-NH3
343.49

Fig. 4

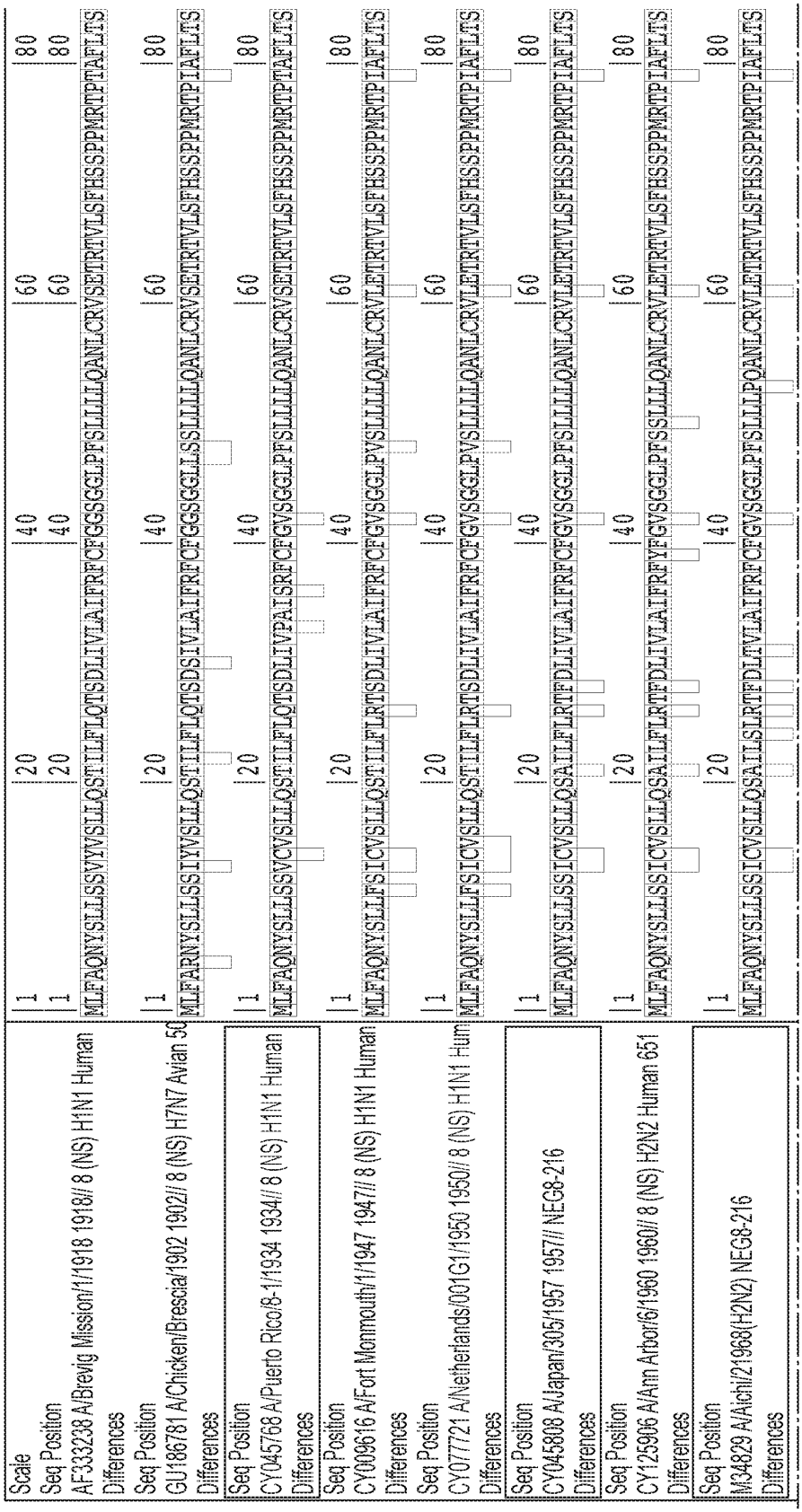

Scale
Seq Position
AF333238 A/Brevig Mission/1/1918 1918// 8 (NS) H1N1 Human
Differences
Seq Position
GU186781 A/Chicken/Brescia/1902 1902// 8 (NS) H7N7 Avian 50
Differences
Seq Position
CY045768 A/Puerto Rico/8-1/1934 1934// 8 (NS) H1N1 Human
Differences
Seq Position
CY009616 A/Fort Monmouth/1/1947 1947// 8 (NS) H1N1 Human
Differences
Seq Position
CY077721 A/Netherlands/001G1/1950 1950// 8 (NS) H1N1 Hum
Differences
Seq Position
CY045808 A/Japan/305/1957 1957// NEG8-216
Differences
Seq Position
CY125906 A/Ann Arbor/6/1960 1960// 8 (NS) H2N2 Human 651
Differences
Seq Position
M34829 A/Aichi/2/1968(H2N2) NEG8-216
Differences

Fig. 4 (Cont. I)

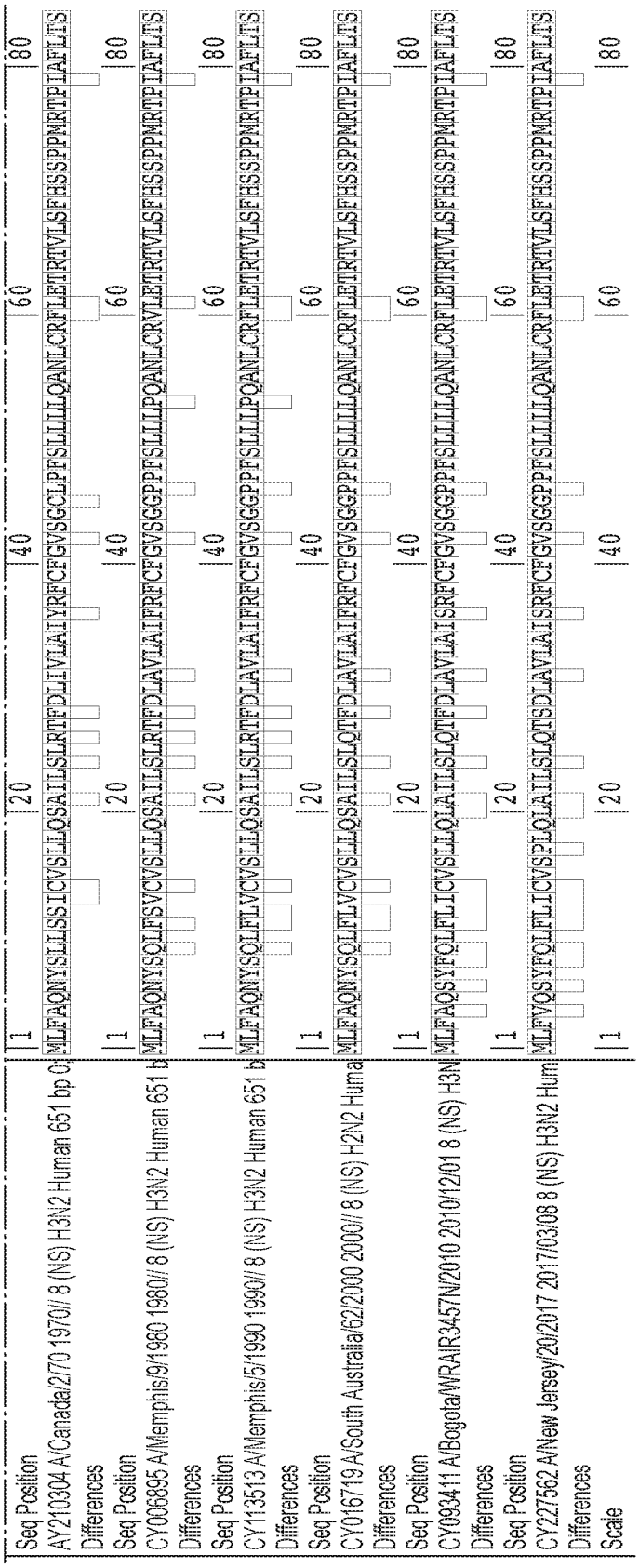

Seq Position
AY210304 A/Canada/2/70 1970// 8 (NS) H3N2 Human 651 bp 0
Differences
Seq Position
CY006895 A/Memphis/9/1980 1980// 8 (NS) H3N2 Human 651 b
Differences
Seq Position
CY113513 A/Memphis/5/1990 1990// 8 (NS) H3N2 Human 651 b
Differences
Seq Position
CY016719 A/South Australia/62/2000 2000// 8 (NS) H2N2 Huma
Differences
Seq Position
CY093411 A/Bogota/WRAIR3457N/2010 2010/12/01 8 (NS) H3N
Differences
Seq Position
CY227562 A/New Jersey/20/2017 2017/03/08 8 (NS) H3N2 Hum
Differences
Scale
1
20
40
60
80

Fig. 4 (Cont. III)

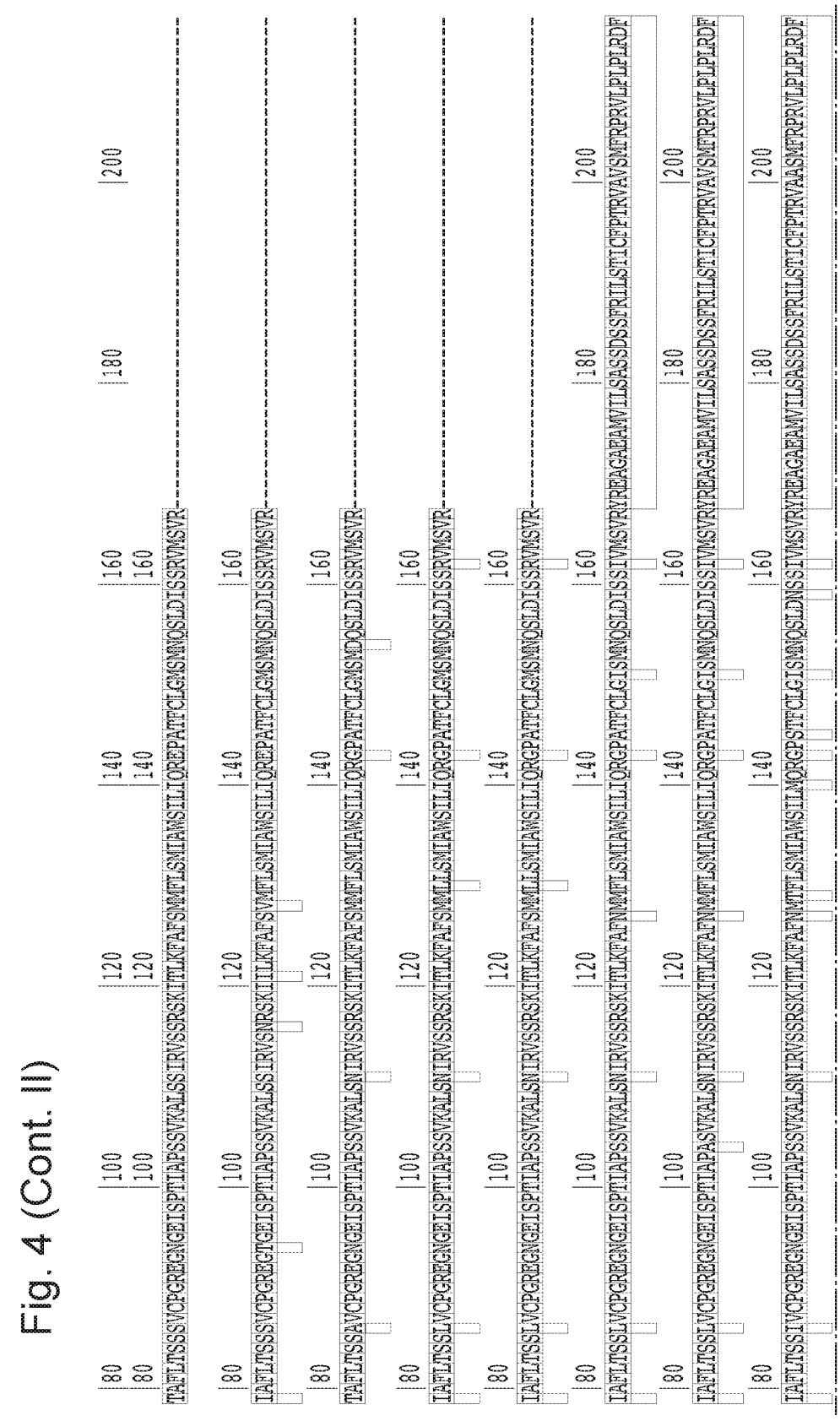


Fig. 4 (Cont. IIII)

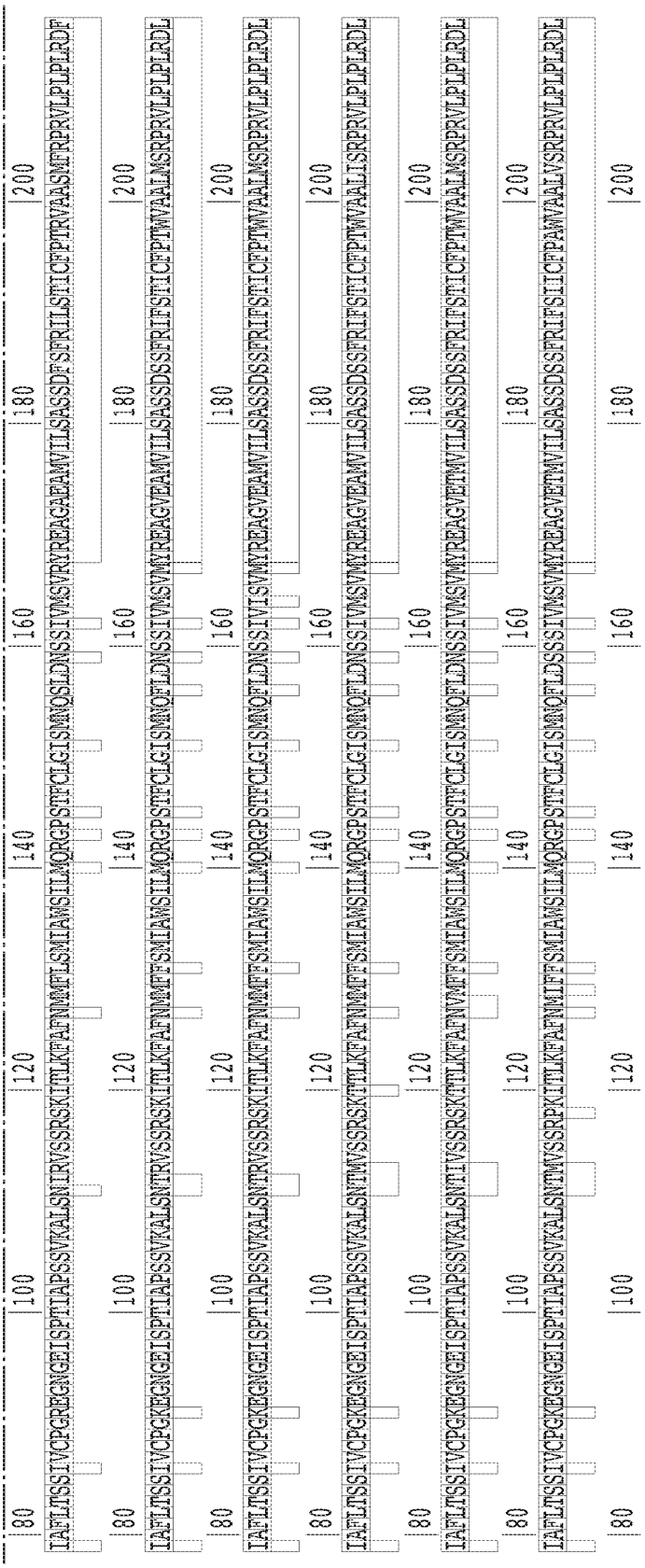


Fig. 5

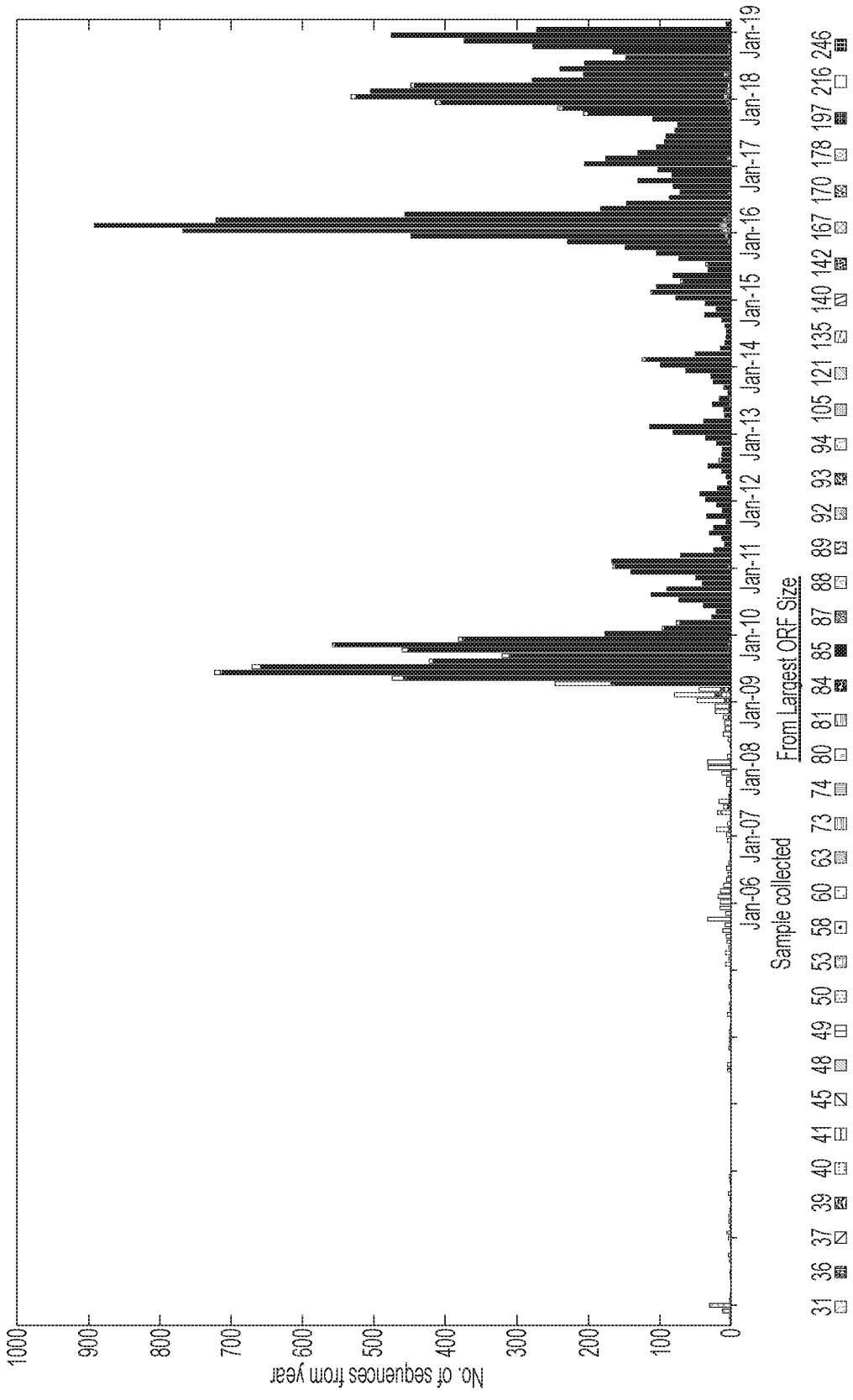

No. of sequences from year
1000
900
800
700
600
500
400
300
200
100
0
Jan-06
Jan-07
Jan-08
Jan-09
Jan-10
Jan-11
Jan-12
Jan-13
Jan-14
Jan-15
Jan-16
Jan-17
Jan-18
Jan-19
Sample collected
From Largest ORF Size
31 36 37 39 40 41 45 48 49 50 53 58 60 63 73 74 80 81 84 85 87 88 89 92 93 94 105 121 135 140 142 167 170 178 197 216 246

Fig. 6

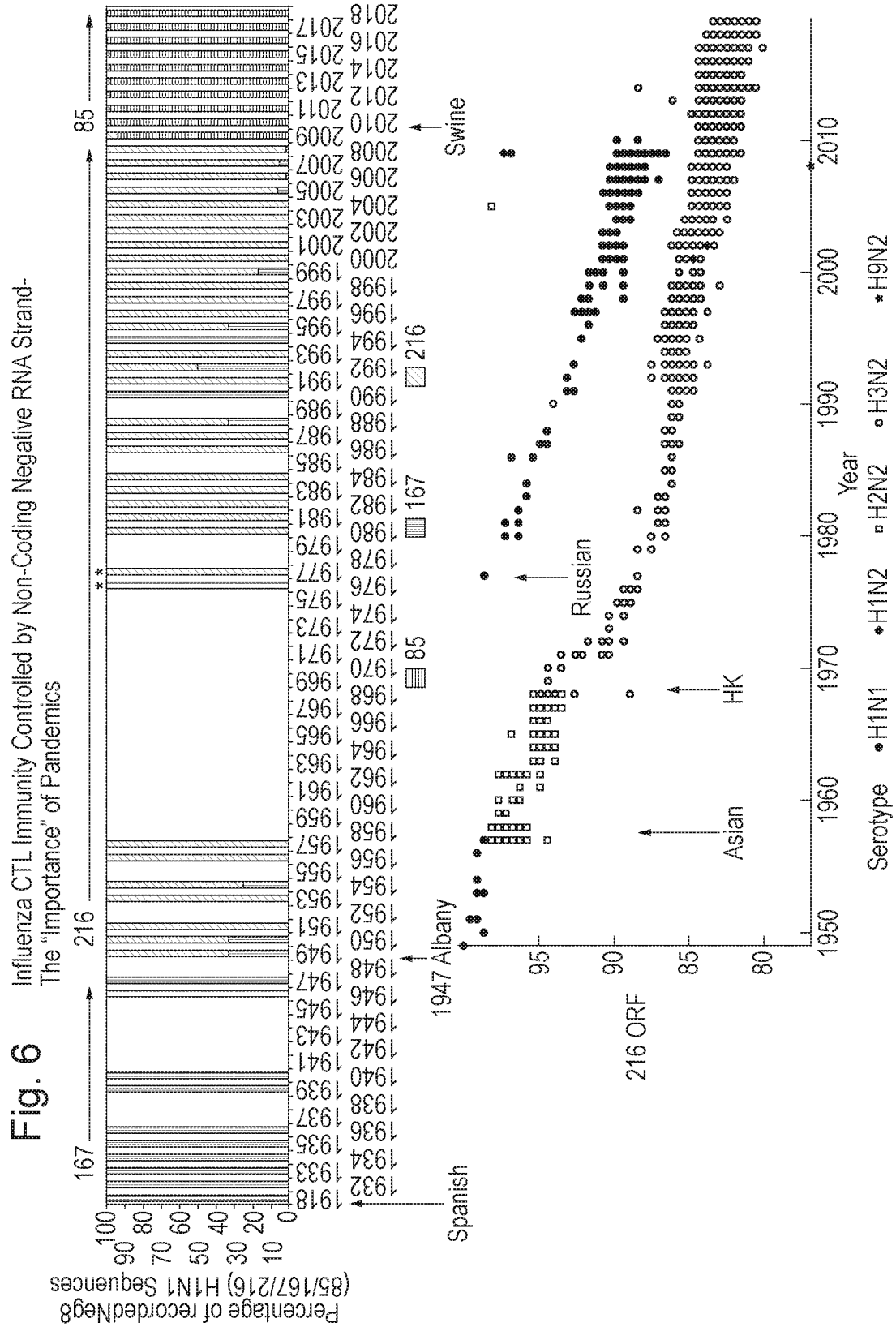

Influenza CTL Immunity Controlled by Non-Coding Negative RNA Strand-
The "Importance" of Pandemics
Percentage of recordedNeg8
(85/167/216) H1N1 Sequences
100
90
80
70
60
50
40
30
20
10
0
167
216
85
**
1918
1932
1933
1934
1935
1936
1937
1938
1939
1940
1941
1942
1943
1944
1945
1946
1947
1948
1949
1950
1951
1952
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2011
2012
2013
2014
2015
2016
2017
2018
85
167
216
Spanish
1947 Albany
Swine
Russian
Asian
HK
216 ORF
95
90
85
80
1950
1960
1970
1980
1990
2000
2010
Year
Serotype
H1N1
H1N2
H2N2
H3N2
H9N2

Fig. 7

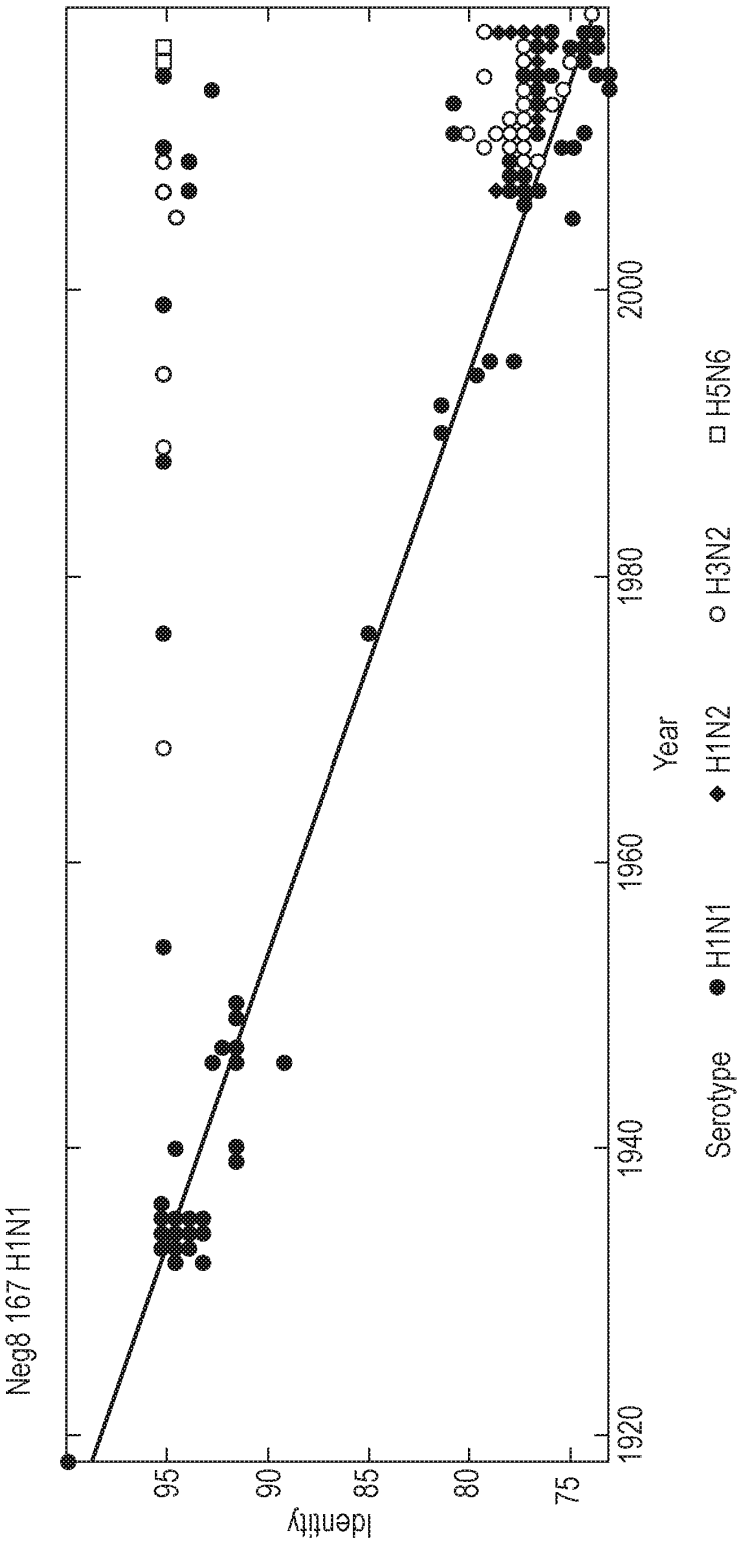
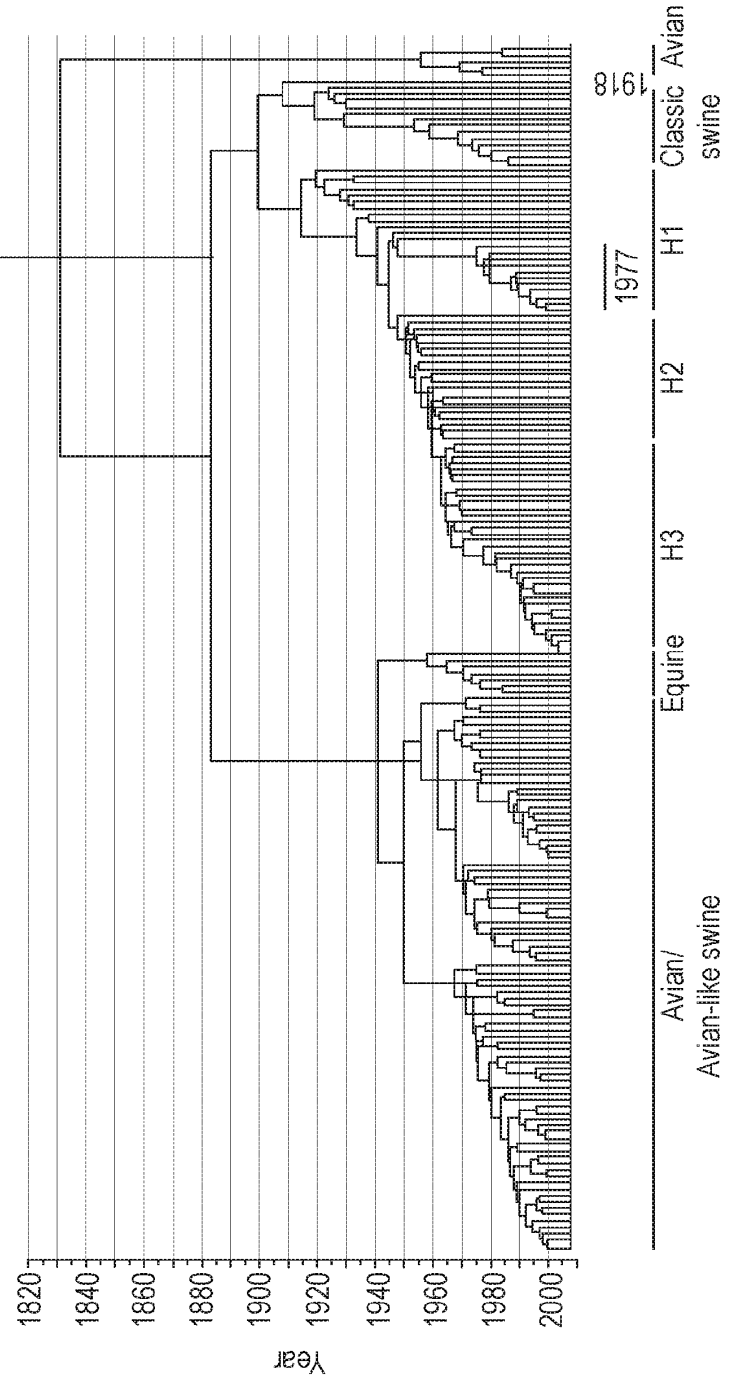

Neg8 167 H1N1
Identity
95
90
85
80
75
1920
1940
1960
1980
2000
Year
Serotype
H1N1
H1N2
H3N2
H5N6

Fig. 8


Humans 216, 167, 85
Avian/Avian-like swine/Equine 93 (rare 135)
Swine 93/135/140/167?
NRG8 ORF
Year
1820
1840
1860
1880
1900
1920
1940
1960
1980
2000
1918
1977
Avian/
Avian-like swine
Equine
H3
H2
H1
Classic
swine
Avian