FIG. 1: HaSMaN Structures vs Matrix M and detergent core HA nanoparticles

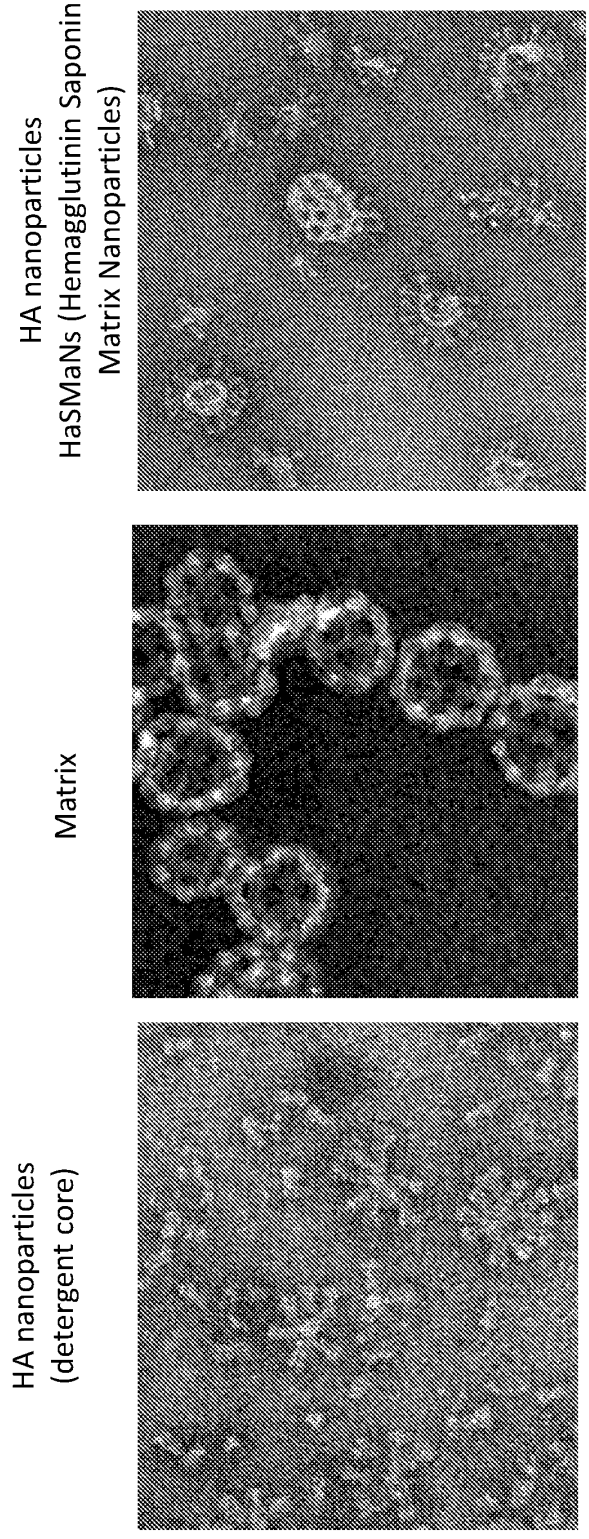


FIG. 2

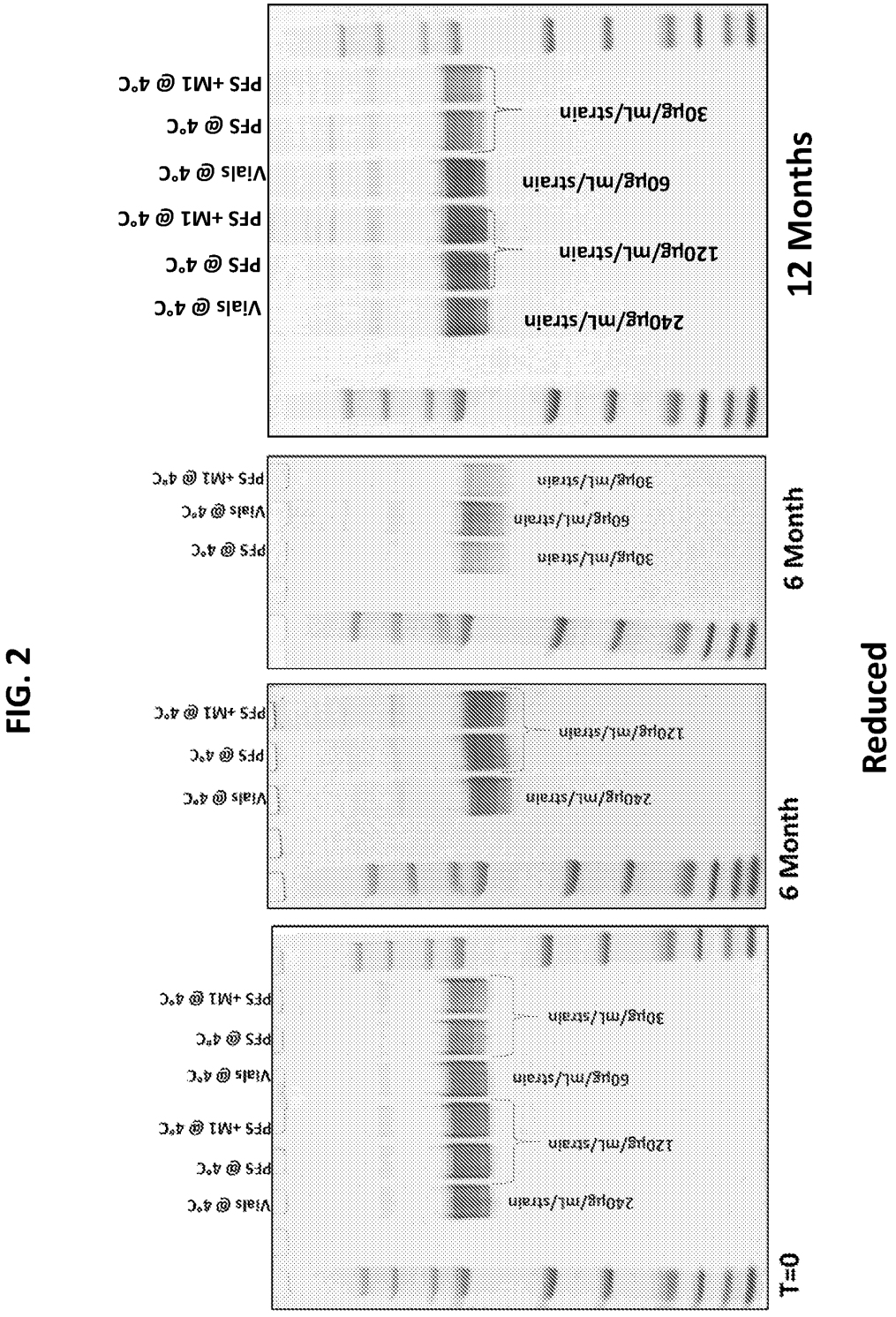

Reduced
T=0
240μg/mL/strain
120μg/mL/strain
60μg/mL/strain
30μg/mL/strain
Vials @ 4°C
PFS @ 4°C
PFS +M1 @ 4°C
Vials @ 4°C
PFS @ 4°C
PFS +M1 @ 4°C
6 Month
240μg/mL/strain
120μg/mL/strain
Vials @ 4°C
PFS @ 4°C
PFS +M1 @ 4°C
6 Month
30μg/mL/strain
60μg/mL/strain
30μg/mL/strain
Vials @ 4°C
PFS @ 4°C
PFS +M1 @ 4°C
12 Months
240μg/mL/strain
120μg/mL/strain
60μg/mL/strain
30μg/mL/strain
Vials @ 4°C
PFS @ 4°C
PFS +M1 @ 4°C

FIG. 3

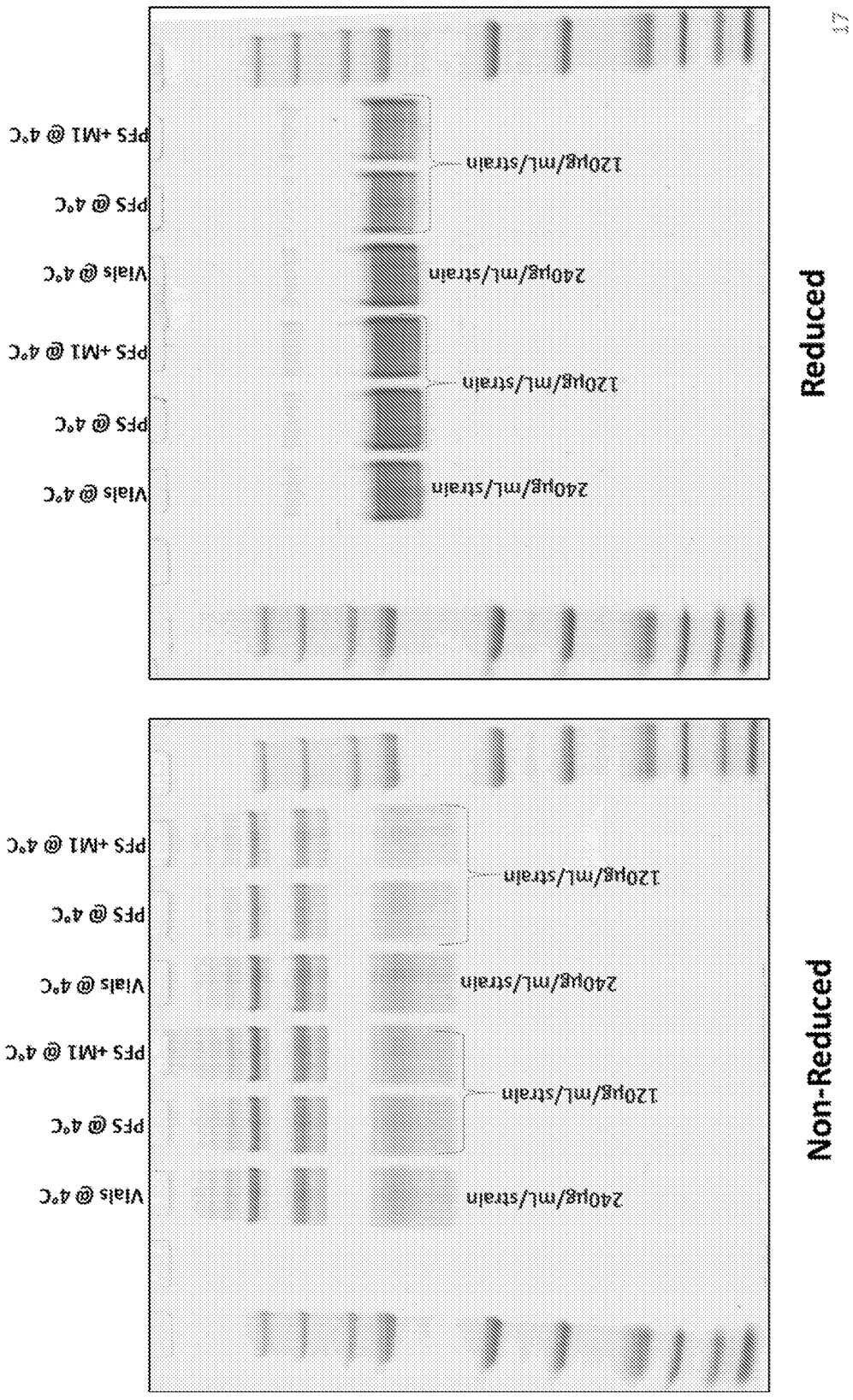

Reduced
240µg/mL/strain
120µg/mL/strain
Vials @ 4°C
PFS @ 4°C
PFS +M1 @ 4°C
240µg/mL/strain
120µg/mL/strain
Vials @ 4°C
PFS @ 4°C
PFS +M1 @ 4°C
Non-Reduced
240µg/mL/strain
120µg/mL/strain
Vials @ 4°C
PFS @ 4°C
PFS +M1 @ 4°C
240µg/mL/strain
120µg/mL/strain
Vials @ 4°C
PFS @ 4°C
PFS +M1 @ 4°C

FIG. 4

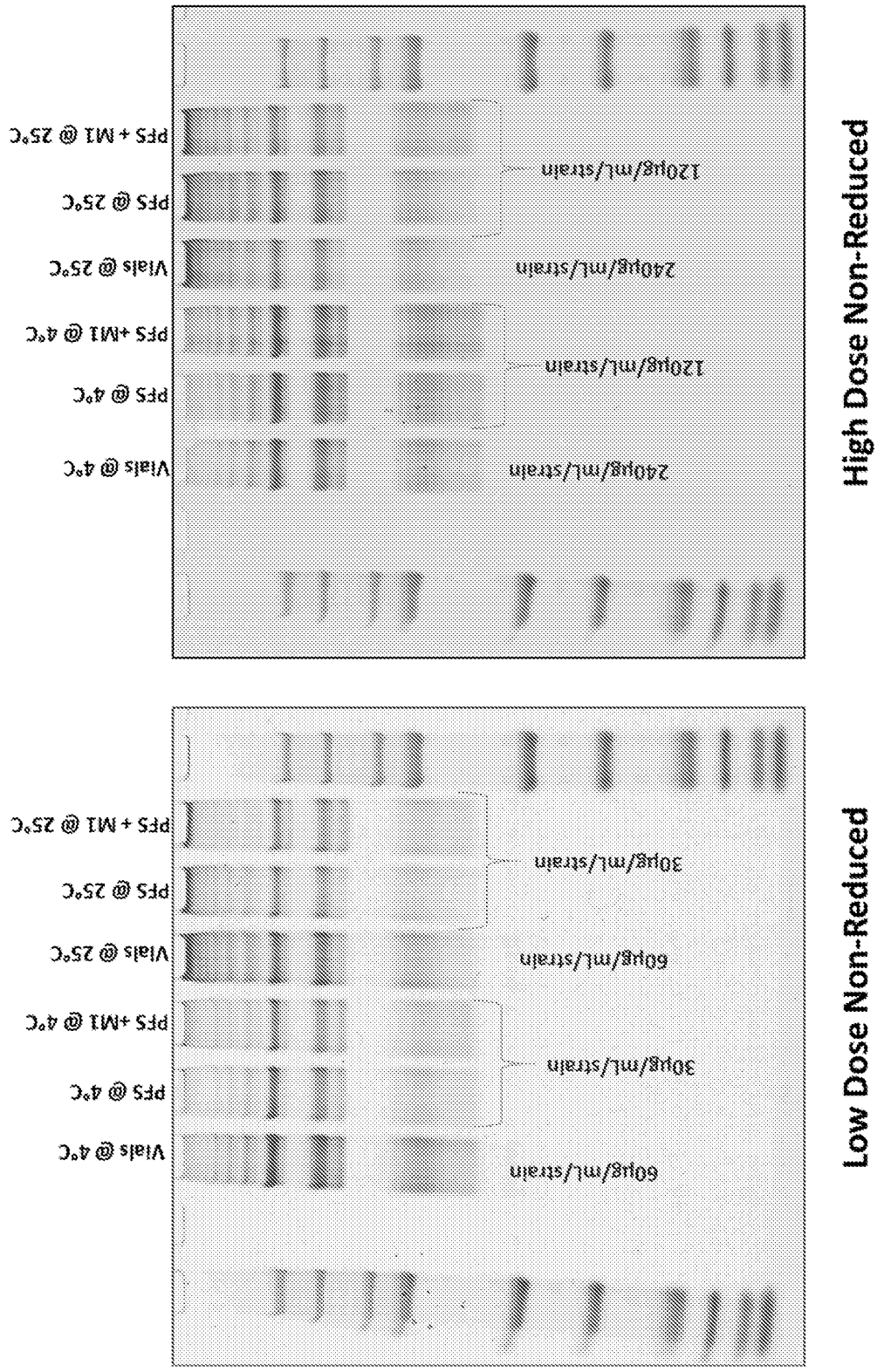

High Dose Non-Reduced
240µg/mL/strain
120µg/mL/strain
240µg/mL/strain
120µg/mL/strain
Vials @ 4°C
PFS @ 4°C
PFS +M1 @ 4°C
Vials @ 25°C
PFS @ 25°C
PFS + M1 @ 25°C
Low Dose Non-Reduced
60µg/mL/strain
30µg/mL/strain
60µg/mL/strain
30µg/mL/strain
Vials @ 4°C
PFS @ 4°C
PFS +M1 @ 4°C
Vials @ 25°C
PFS @ 25°C
PFS + M1 @ 25°C

FIG. 5

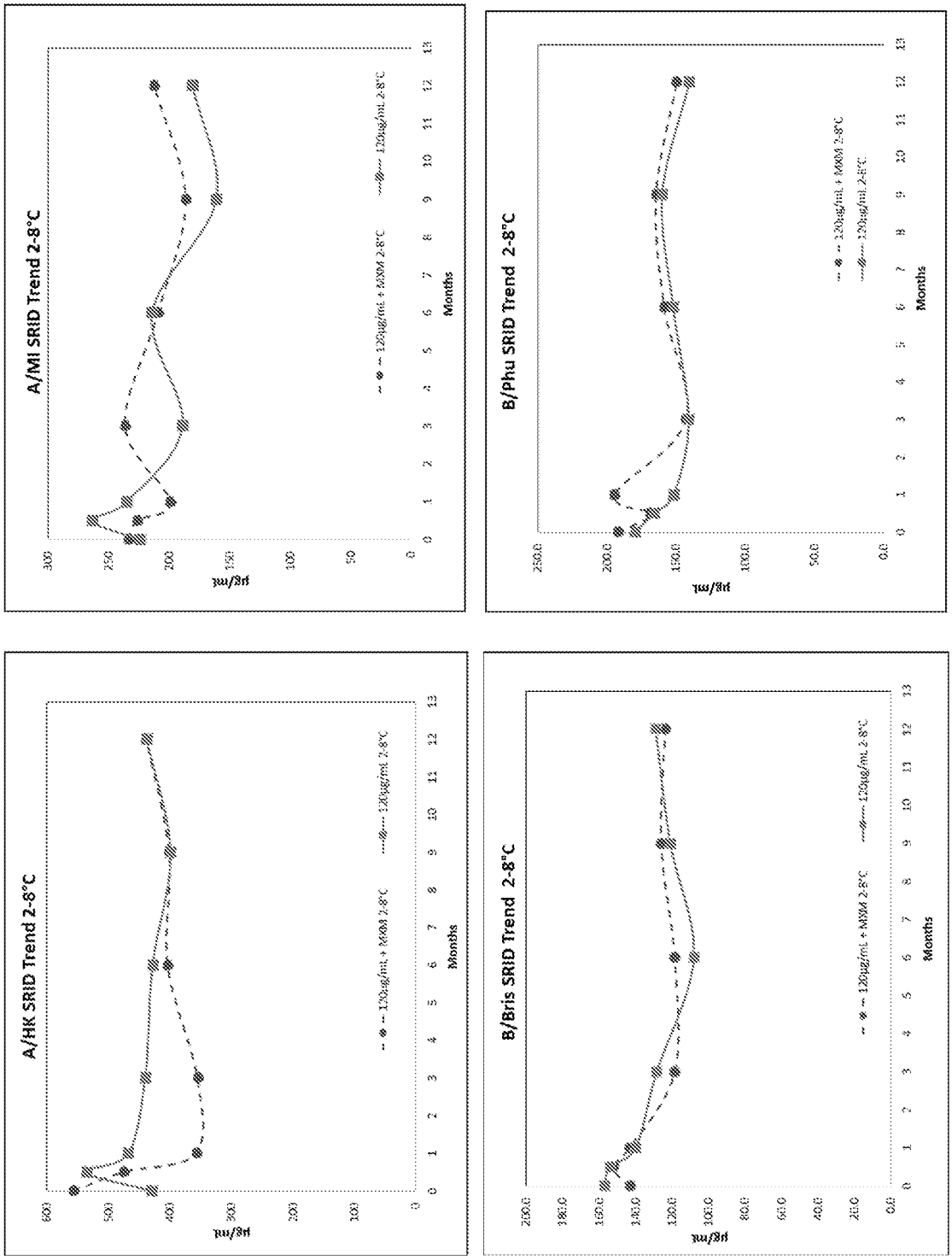

A/MI SRID Trend 2-8°C
A/HK SRID Trend 2-8°C
B/Phu SRID Trend 2-8°C
B/Bris SRID Trend 2-8°C
µg/mL
Months
120µg/mL + MXM 2-8°C
120µg/mL 2-8°C

FIG. 6

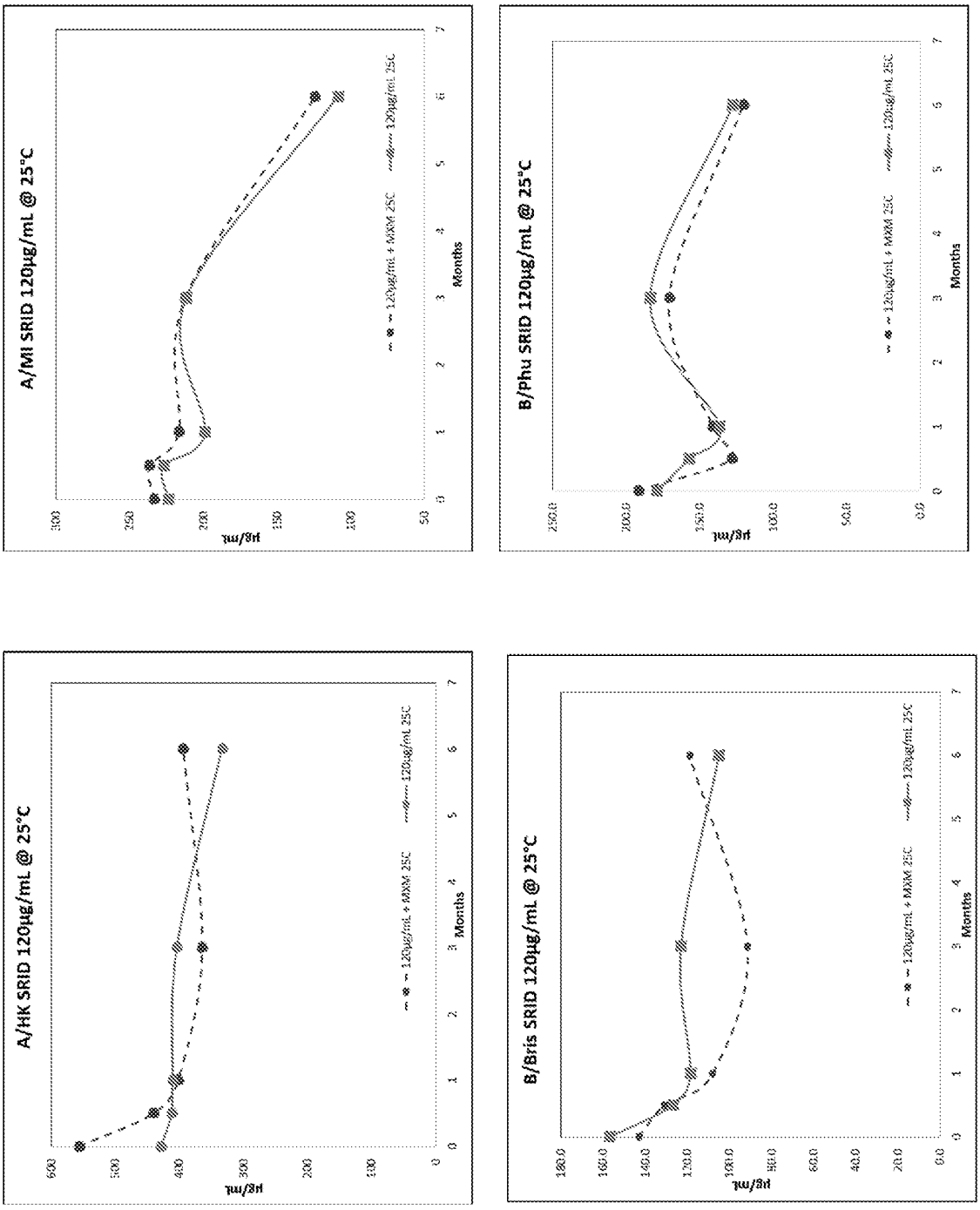

A/MI SRID 120µg/mL @ 25°C
µg/mL
Months
120µg/mL + MXM 25C
120µg/mL 25C
A/HK SRID 120µg/mL @ 25°C
µg/mL
Months
120µg/mL + MXM 25C
120µg/mL 25C
B/Phu SRID 120µg/mL @ 25°C
µg/mL
Months
120µg/mL + MXM 25C
120µg/mL 25C
B/Bris SRID 120µg/mL @ 25°C
µg/mL
Months
120µg/mL + MXM 25C
120µg/mL 25C

FIG. 7

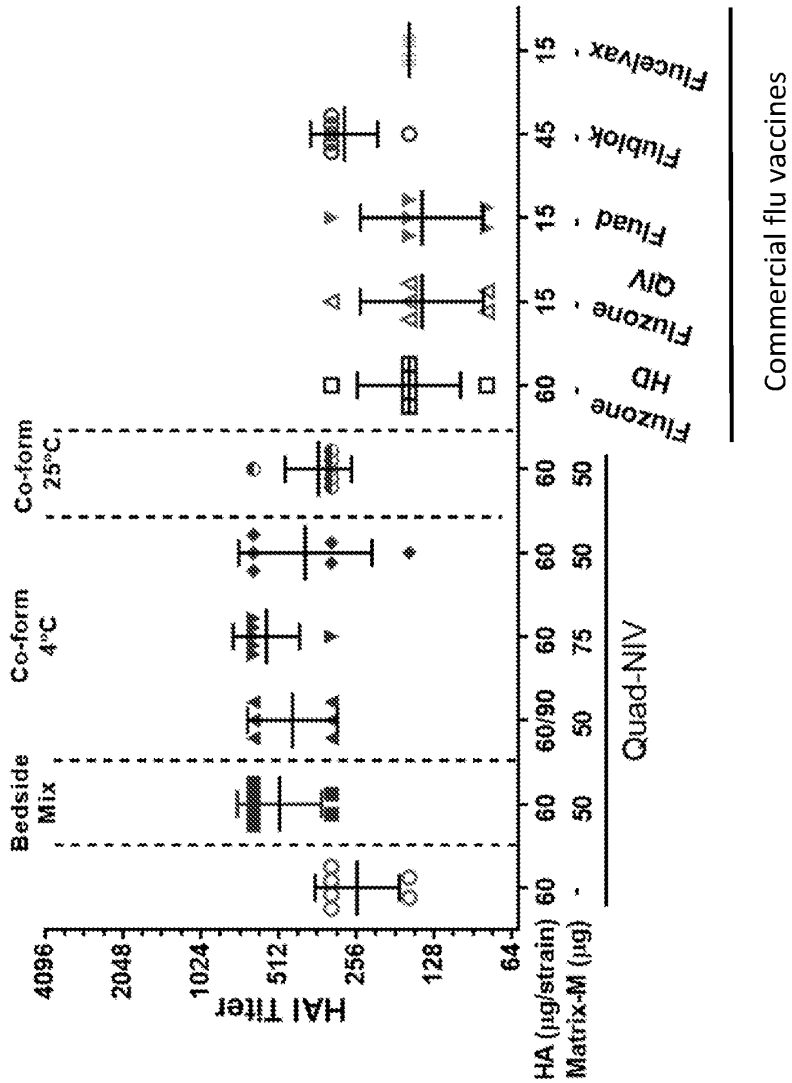

A/Hong Kong/4801/2014
HAI Titer
4096
2048
1024
512
256
128
64
Bedside Mix
Co-form 4°C
Co-form 25°C
HA (µg/strain)
Matrix-M (µg)
60 - 60 50 60/90 50 60 75 60 50 60 50
Quad-NIV
Fluzone HD 60 -
Fluzone QIV 15 -
Fluad 15 -
Flublok 45 -
FluceIvax 15 -
Commercial flu vaccines

FIG. 8

A/Michigan/45/2015

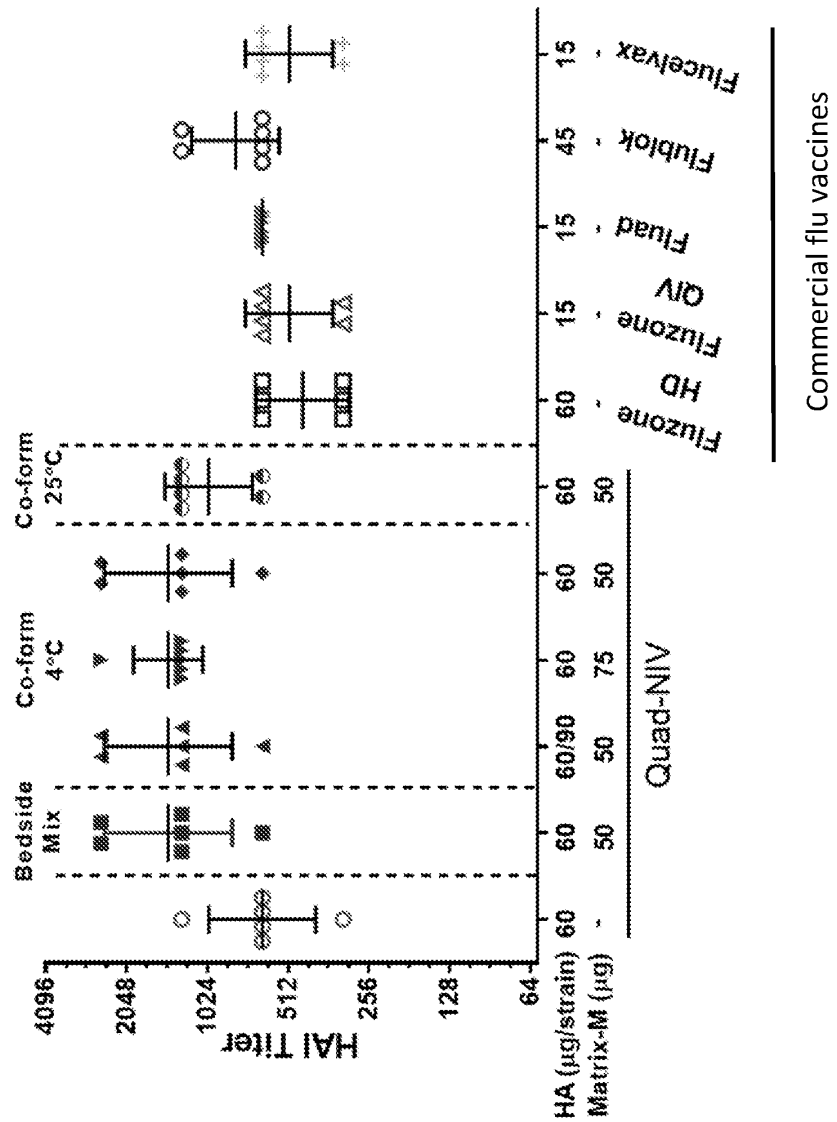


FIG. 9

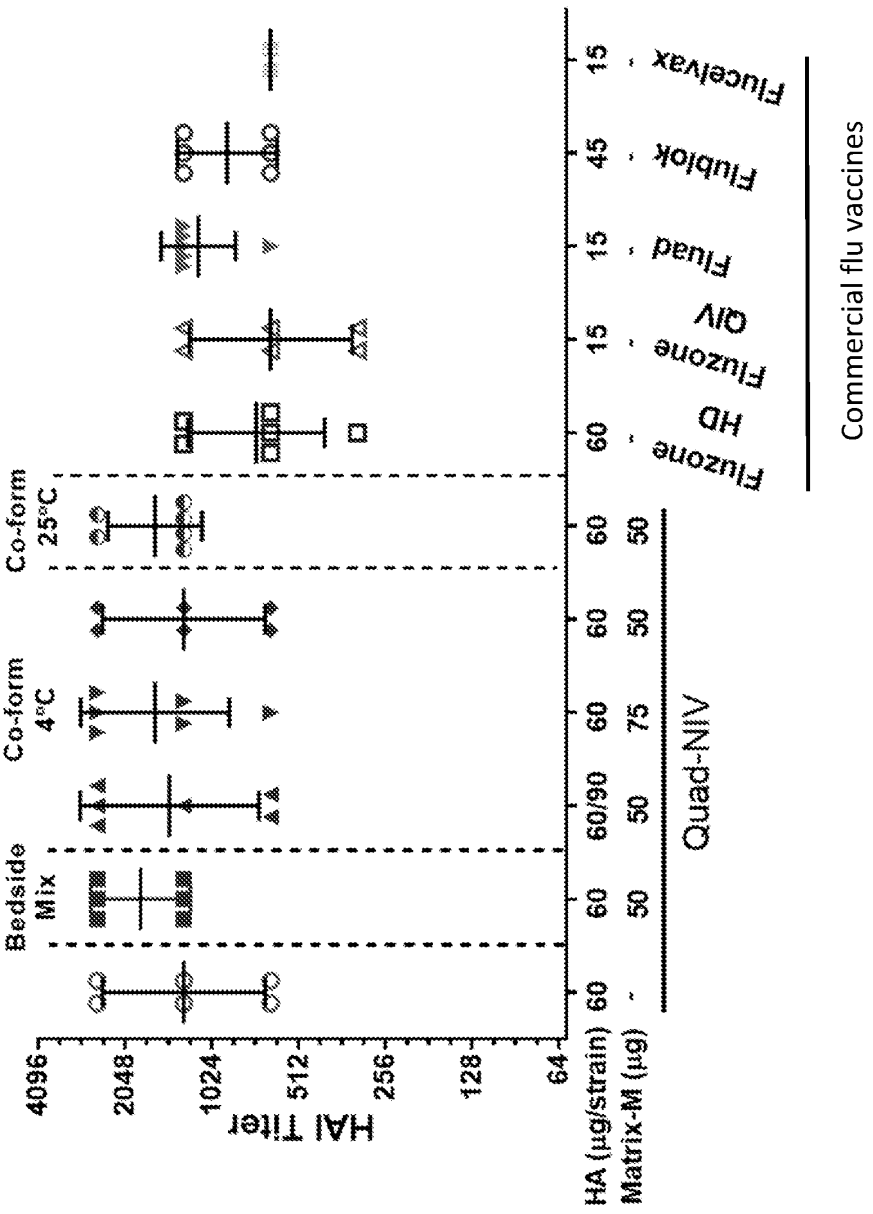

B/Brisbane/60/2008
HAI Titer
4096
2048
1024
512
256
128
64
Bedside Mix
Co-form 4°C
Co-form 25°C
HA (µg/strain) 60 60 60/90 60 60 60
Matrix-M (µg) - 50 50 75 50 50
Quad-NIV
Fluzone HD
Fluzone QIV
Fluad
Flublok
Flucelvax
15 60 15 15 45 15
Commercial flu vaccines

FIG. 10

B/Phuket/3073/2013

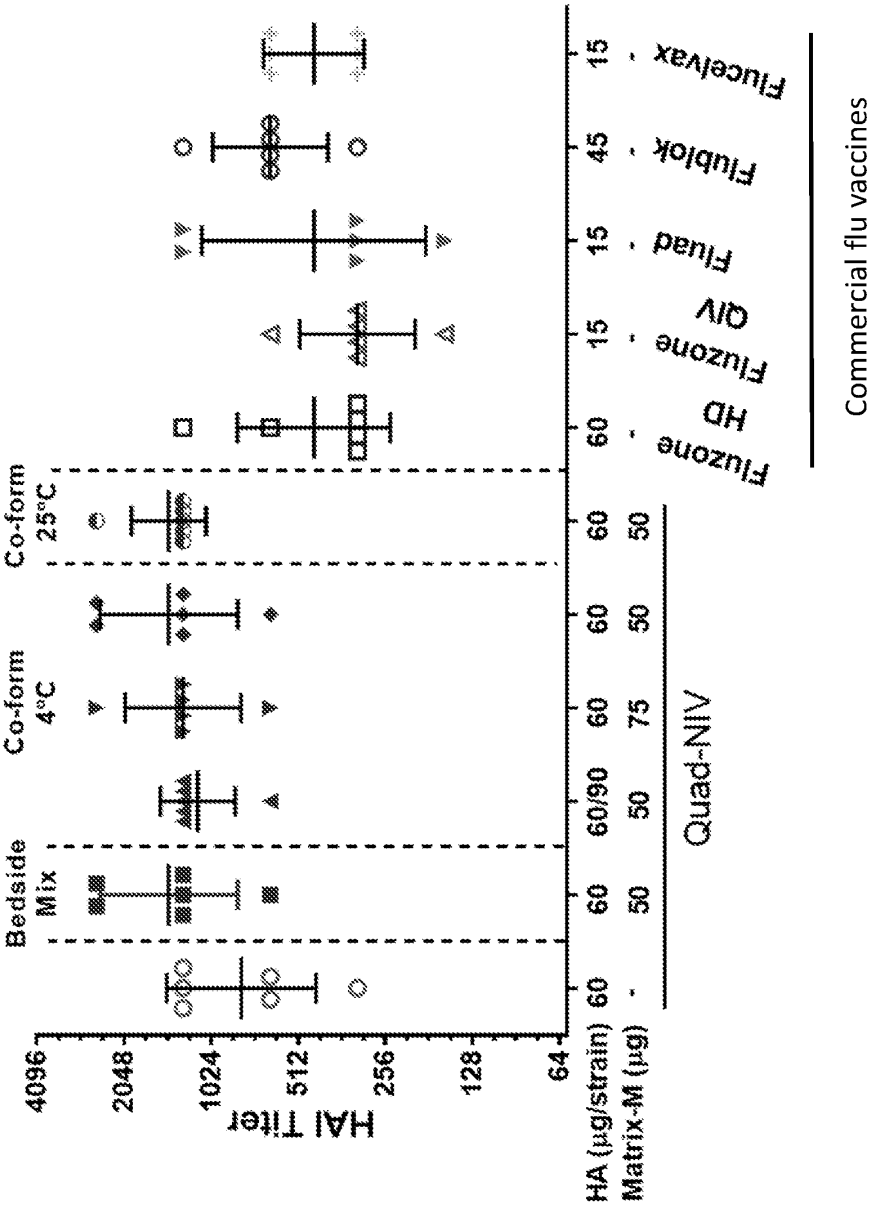


FIG. 11

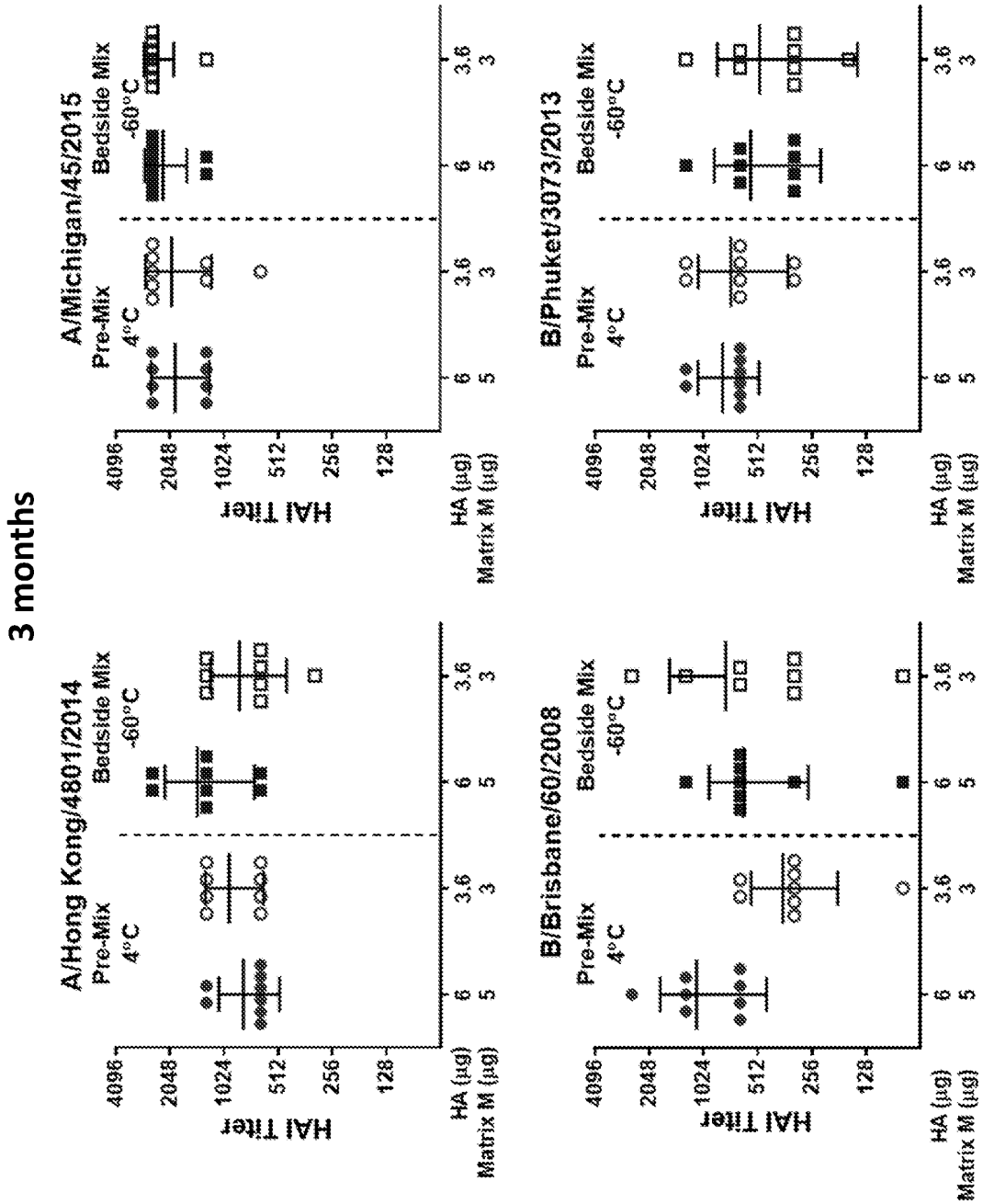

3 months
A/Hong Kong/4801/2014
A/Michigan/45/2015
B/Brisbane/60/2008
B/Phuket/3073/2013
Pre-Mix
Bedside Mix
4°C
-60°C
HAI Titer
4096
2048
1024
512
256
128
HA (µg)
Matrix M (µg)
6
3.6
5
3

FIG. 12

6 months

Day 21 A/Michigan Strains

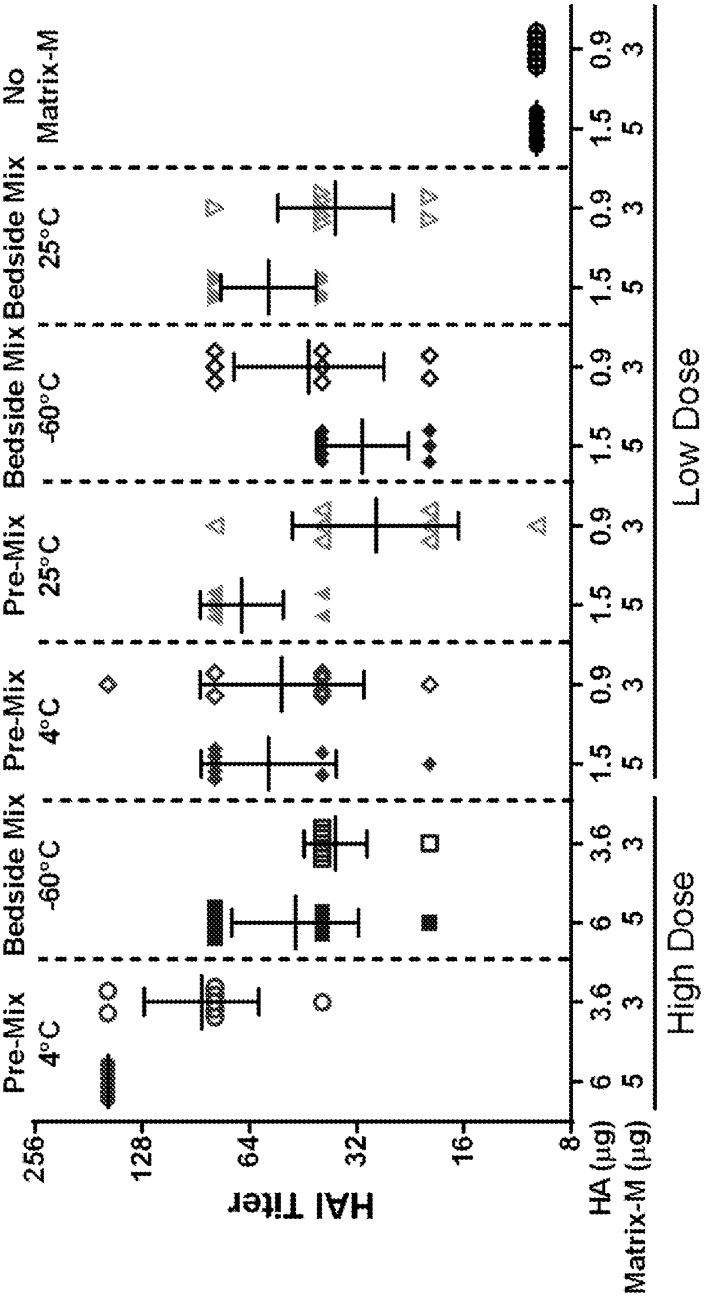


FIG. 13

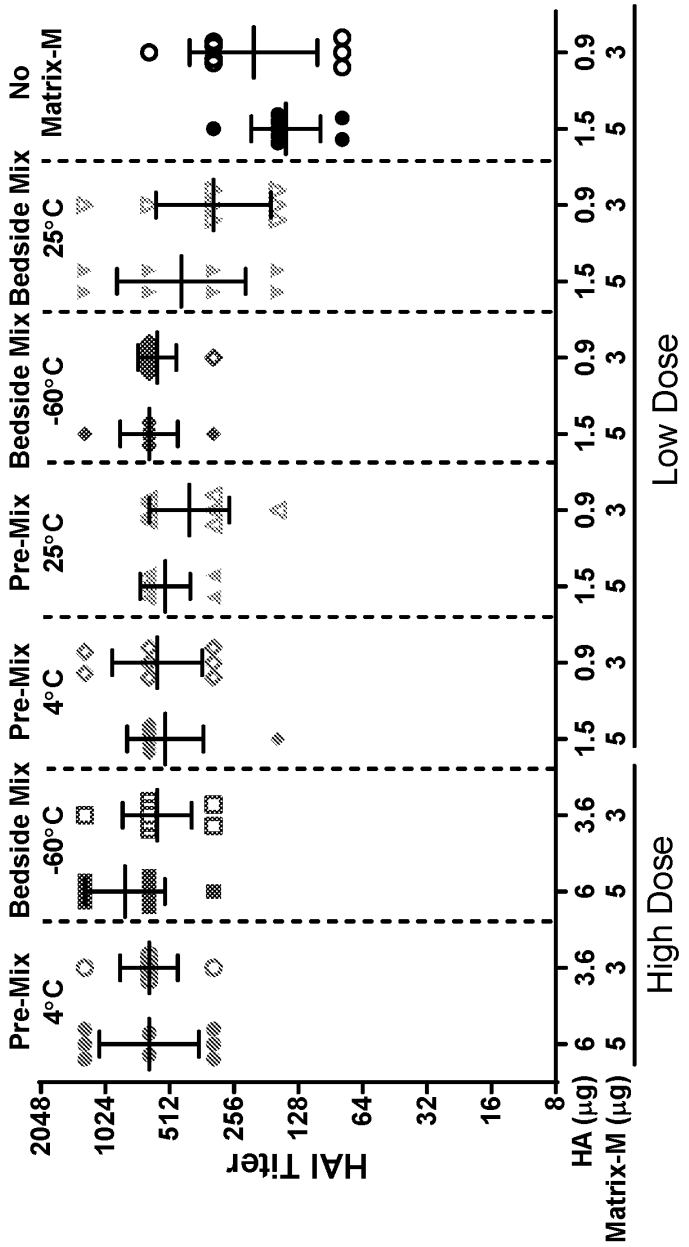

6 months
Day 35 A/Michigan Strains
HAI Titer
2048
1024
512
256
128
64
32
16
8
HA (µg)
Matrix-M (µg)
5 6 3.6 1.5 0.9
3 5 6 3 5
Pre-Mix 4°C
Bedside Mix -60°C
Pre-Mix 4°C
Pre-Mix 25°C
Bedside Mix -60°C
Bedside Mix 25°C
No Matrix-M
High Dose
Low Dose

FIG. 14

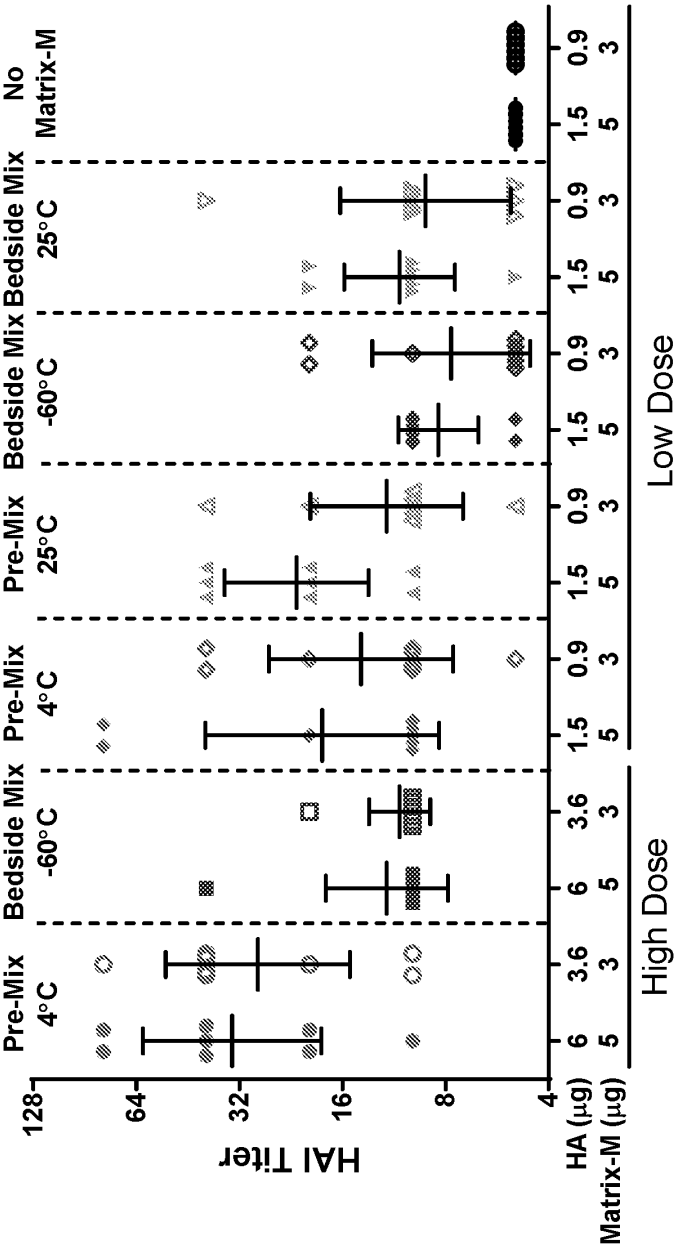

6 months
Day 21 A/Hong Kong Strain
HAI Titer
128
64
32
16
8
4
Pre-Mix 4°C
Bedside Mix -60°C
Pre-Mix 4°C
Pre-Mix 25°C
Bedside Mix -60°C
Bedside Mix 25°C
No Matrix-M
HA (µg)
Matrix-M (µg)
5 6 3.6 3 5 6 3.6 3 1.5 5 0.9 3 1.5 5 0.9 3 1.5 5 0.9 3 1.5 5 0.9 3
High Dose
Low Dose

FIG. 15

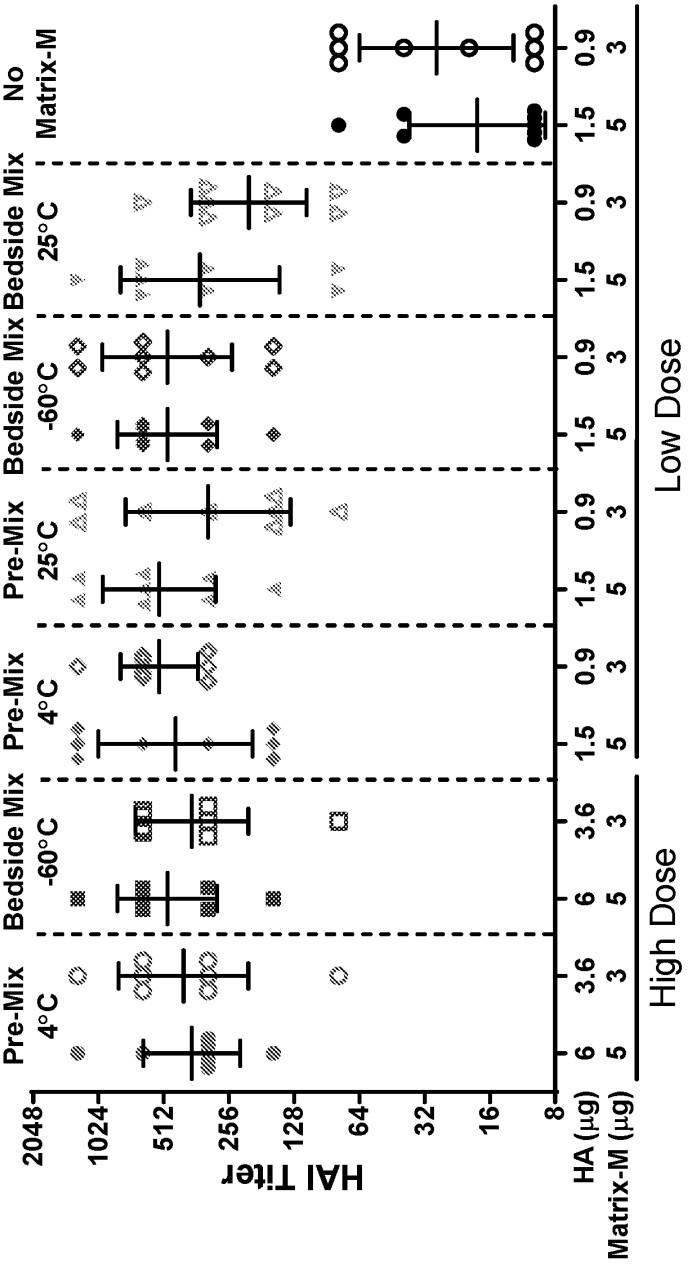

6 months
Day 35 A/Hong Kong Strains
HAI Titer
2048
1024
512
256
128
64
32
16
8
Pre-Mix 4°C
Bedside Mix -60°C
Pre-Mix 4°C
Pre-Mix 25°C
Bedside Mix -60°C
Bedside Mix 25°C
No Matrix-M
HA (µg)
Matrix-M (µg)
6 3.6 6 3.6 1.5 0.9 1.5 0.9 1.5 0.9 1.5 0.9
5 3 5 3 5 3 5 3 5 3 5 3
High Dose
Low Dose

FIG. 16

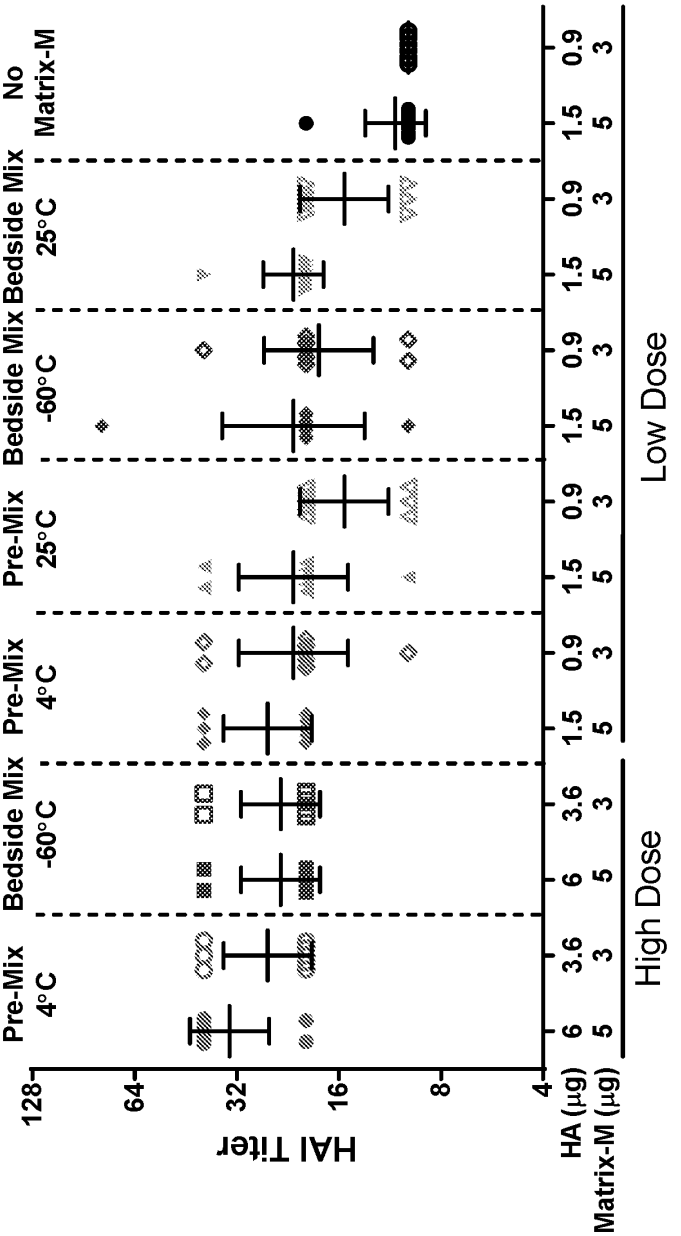

6 months
Day 21 B/Brisbane Strains
HAI Titer
128
64
32
16
8
4
Pre-Mix 4°C
Bedside Mix -60°C
Pre-Mix 4°C
Pre-Mix 25°C
Bedside Mix -60°C
Bedside Mix 25°C
No Matrix-M
HA (µg)
Matrix-M (µg)
6 3.6 1.5 0.9
5 3 5 3
High Dose
Low Dose

FIG. 17

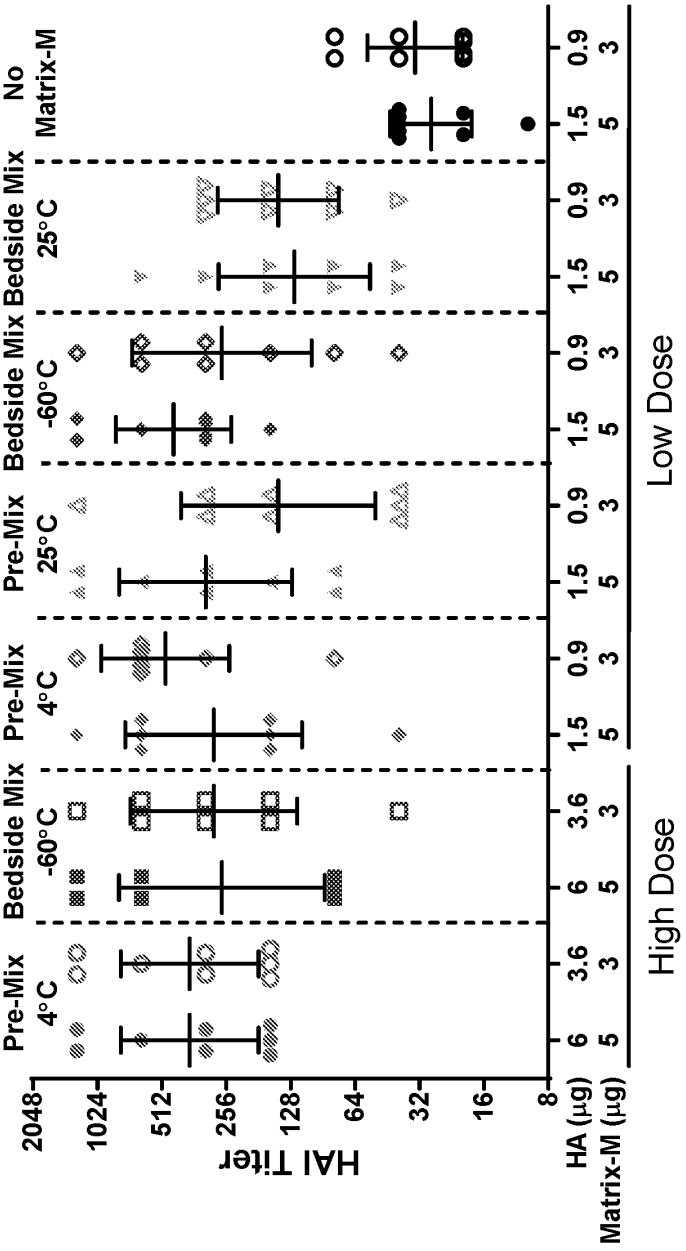

6 months
Day 35 B/Brisbane Strains
HAI Titer
2048
1024
512
256
128
64
32
16
8
Pre-Mix 4°C
Bedside Mix -60°C
Pre-Mix 4°C
Pre-Mix 25°C
Bedside Mix -60°C
Bedside Mix 25°C
No Matrix-M
HA (µg)
Matrix-M (µg)
5 6 3.6 3 5 6 3.6 3 1.5 5 0.9 3 1.5 5 0.9 3 1.5 5 0.9 3 1.5 5 0.9 3
High Dose
Low Dose

FIG. 18

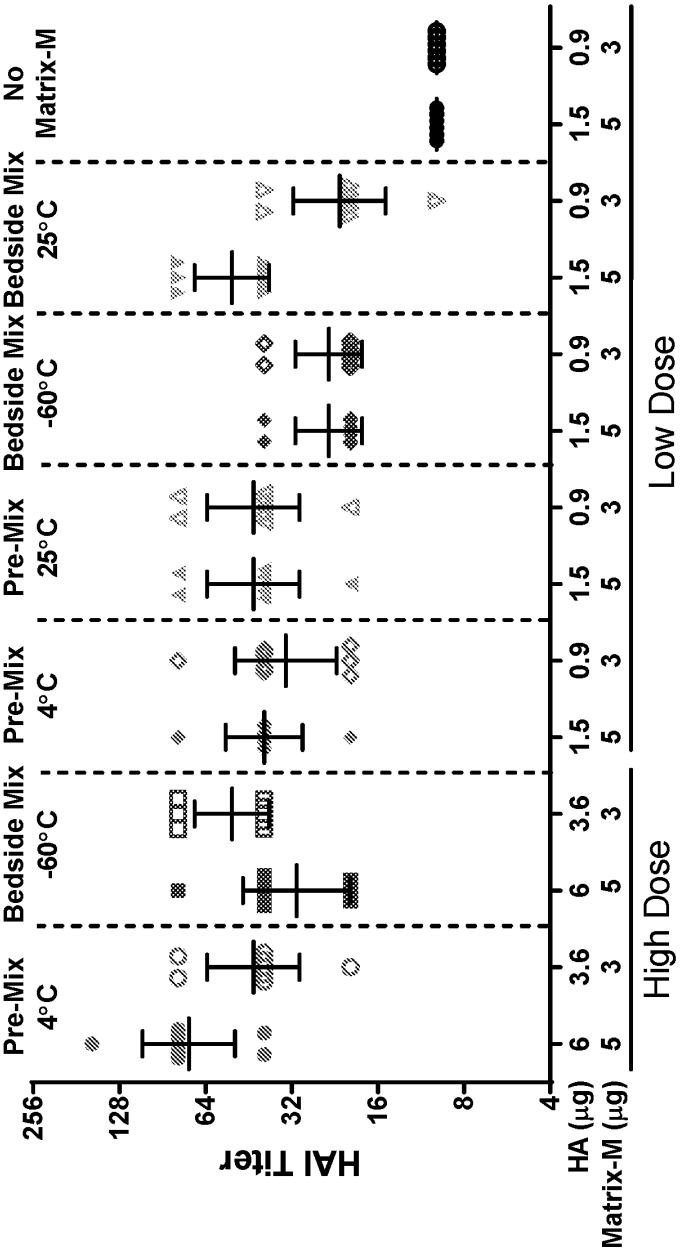

6 months
Day 21 B/Phuket Strains
HAI Titer
256
128
64
32
16
8
4
Pre-Mix 4°C
Bedside Mix -60°C
Pre-Mix 4°C
Pre-Mix 25°C
Bedside Mix -60°C
Bedside Mix 25°C
No Matrix-M
HA (µg) 6 3.6 6 3.6 5 1.5 5 1.5 0.9 3 0.9 3 1.5 5 1.5 5 0.9 3
Matrix-M (µg) 5 3 5 3 5 1.5 5 1.5 0.9 3 0.9 3 1.5 5 1.5 5 0.9 3
High Dose
Low Dose

FIG. 19

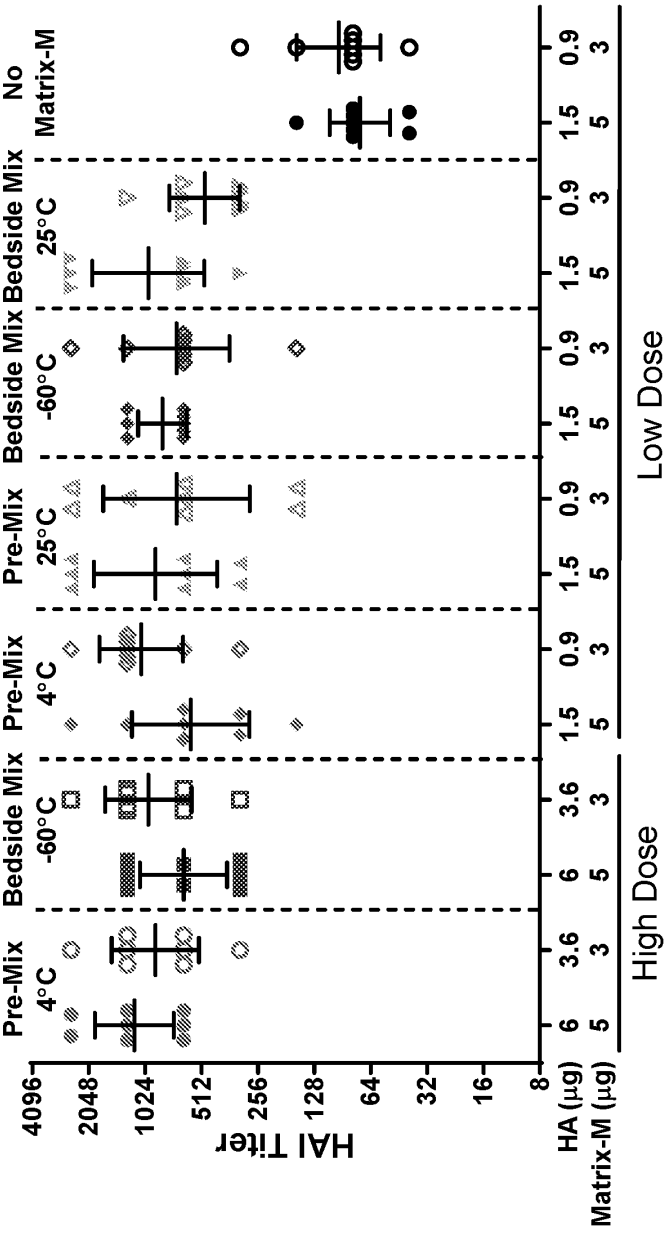

6 months
Day 35 B/Phuket Strains
HAI Titer
4096
2048
1024
512
256
128
64
32
16
8
Pre-Mix 4°C
Bedside Mix -60°C
Pre-Mix 4°C
Pre-Mix 25°C
Bedside Mix -60°C
Bedside Mix 25°C
No Matrix-M
HA (µg) 5 6 3.6 3 6 5 3.6 3 1.5 5 0.9 3 1.5 5 0.9 3 1.5 5 0.9 3 1.5 5 0.9 3
Matrix-M (µg)
High Dose
Low Dose

FIG. 20

12 months
Day 21 A/Hong Kong Strain

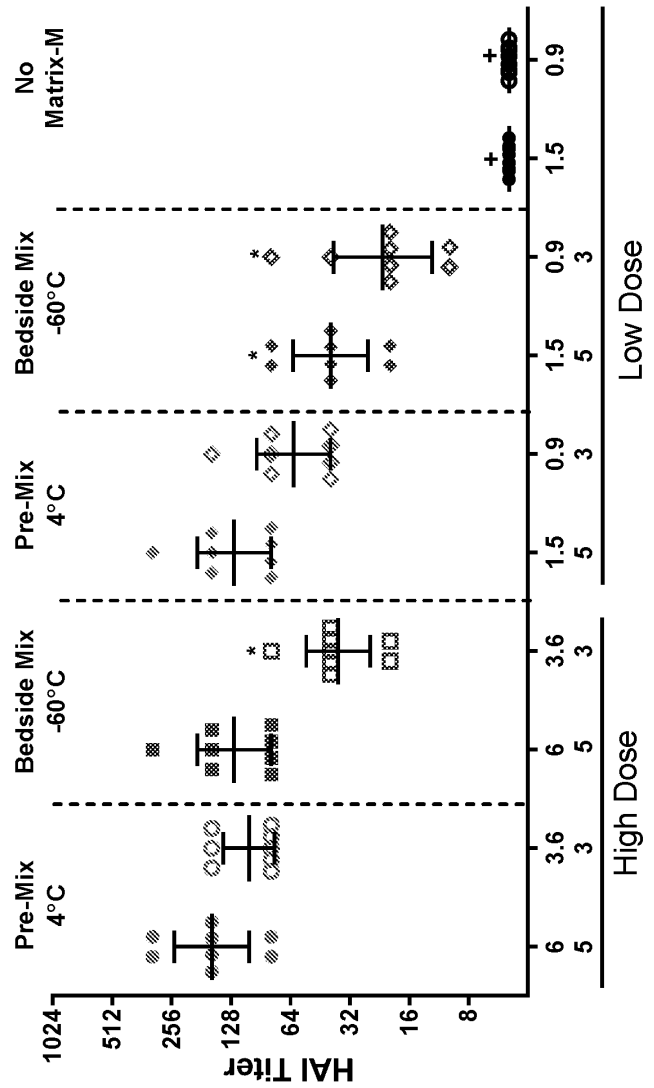


FIG. 21

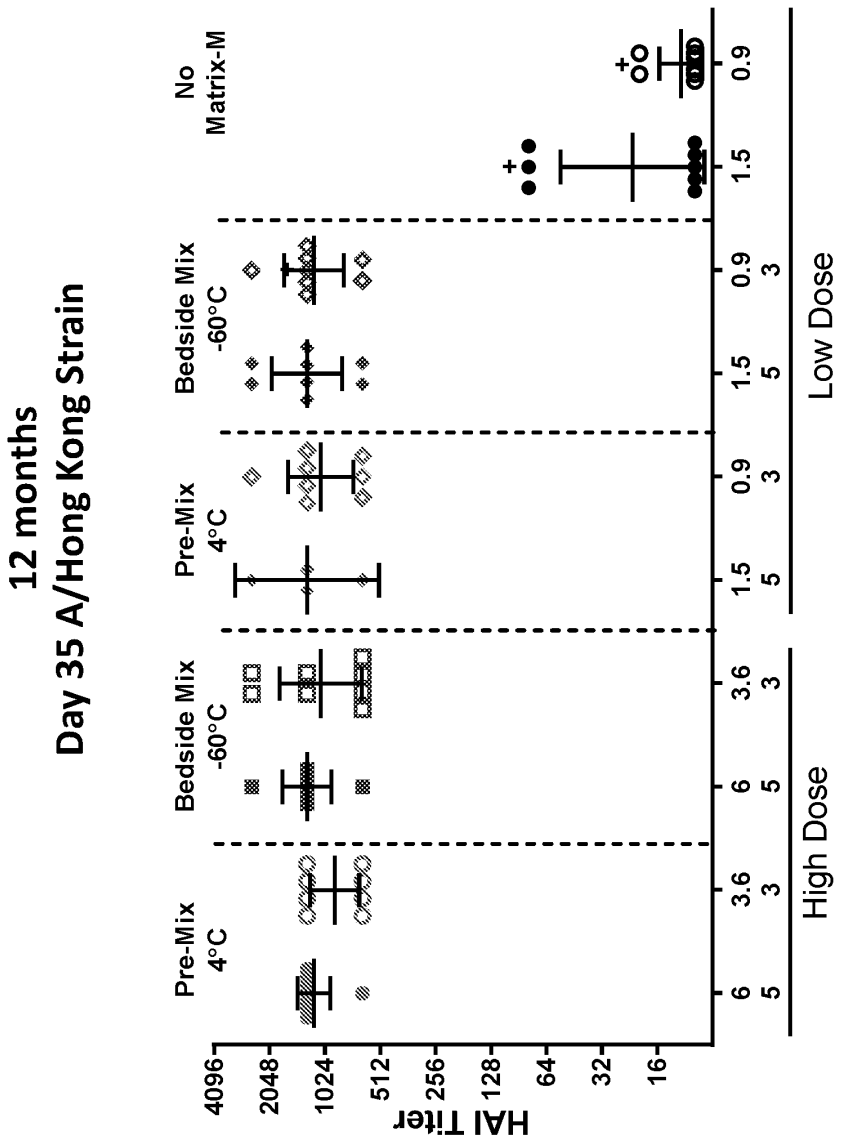

12 months
Day 35 A/Hong Kong Strain
HAI Titer
4096
2048
1024
512
256
128
64
32
16
Pre-Mix 4°C
Bedside Mix -60°C
Pre-Mix 4°C
Bedside Mix -60°C
No Matrix-M
5
6
3.6
3
5
6
3.6
3
5
1.5
0.9
3
5
1.5
0.9
3
5
1.5
0.9
High Dose
Low Dose

FIG. 22

12 months
Day 21 A/Michigan Strain

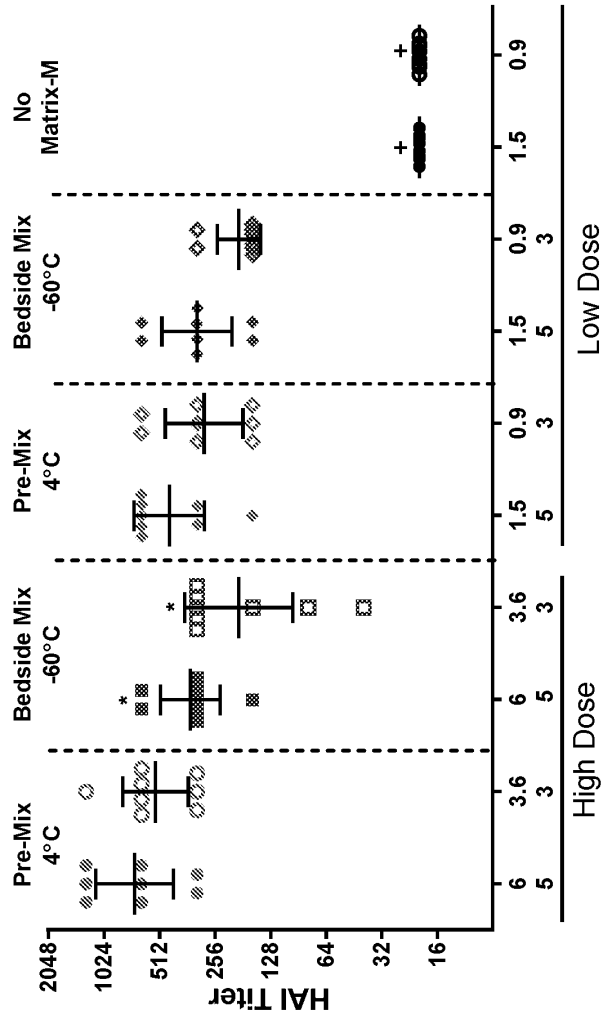


FIG. 23

12 months

Day 35 A/Michigan Strain

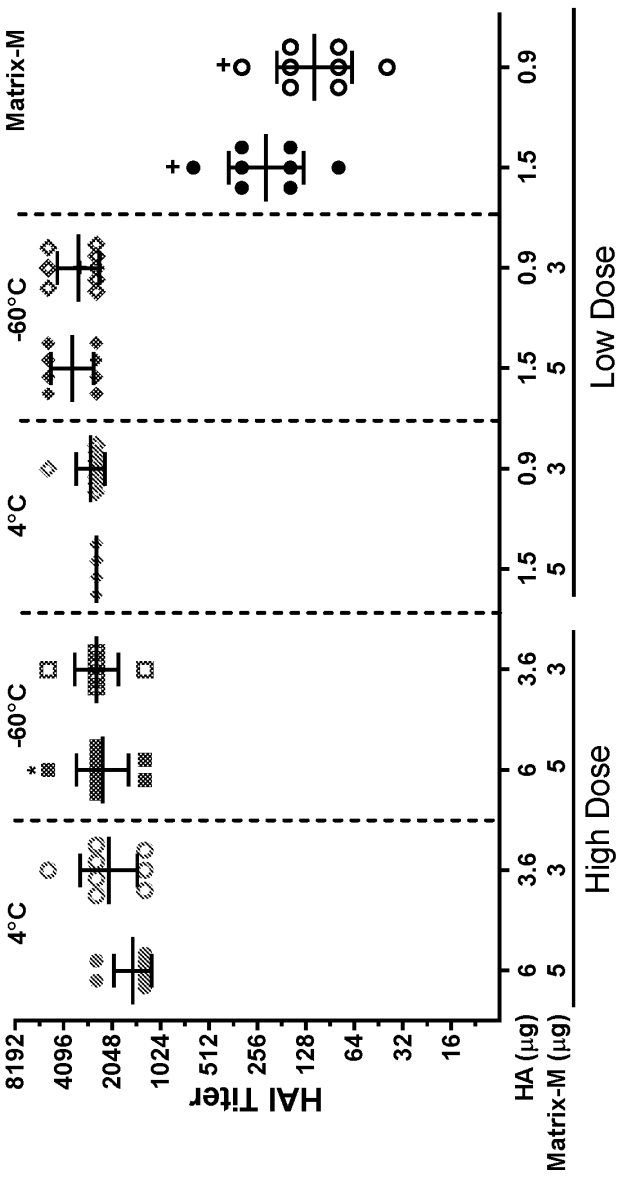


FIG. 24

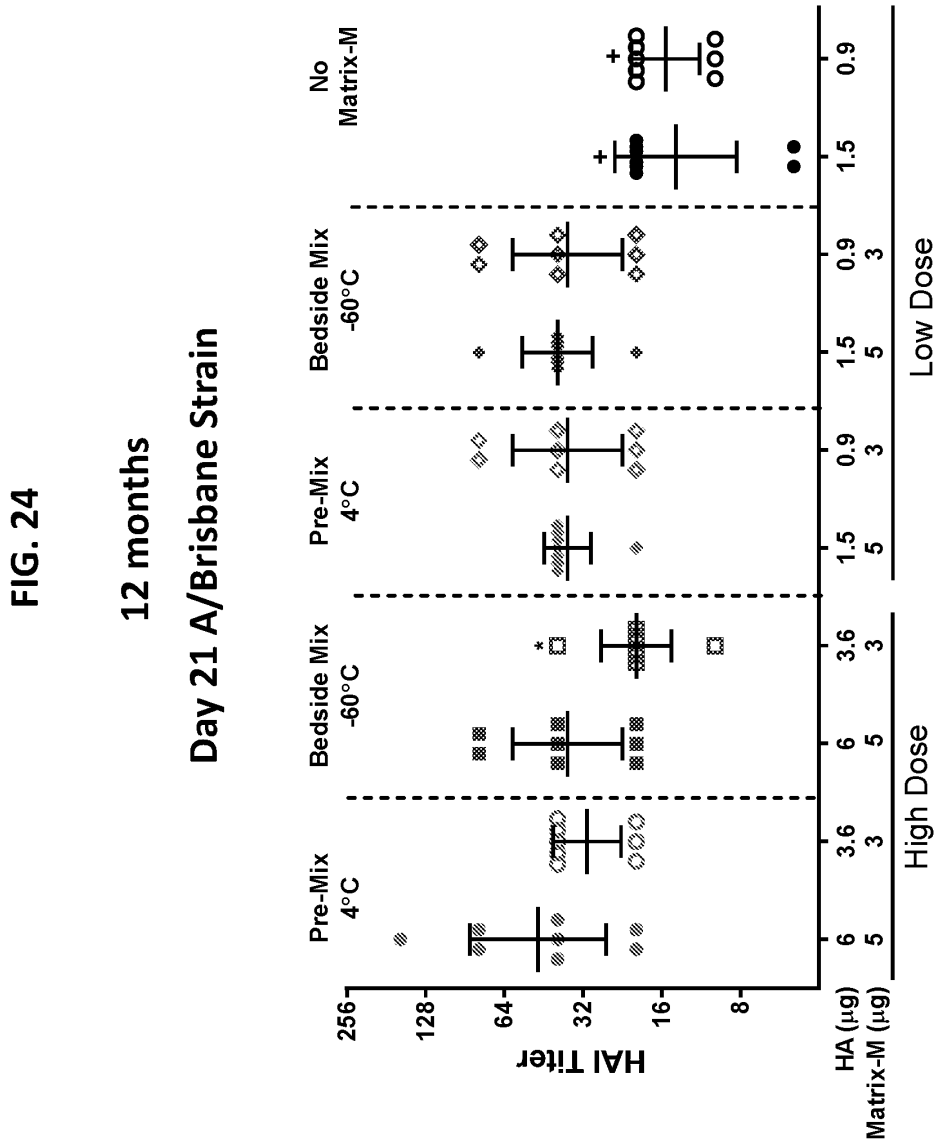

12 months
Day 21 A/Brisbane Strain
HAI Titer
256
128
64
32
16
8
Pre-Mix 4°C
Bedside Mix -60°C
Pre-Mix 4°C
Bedside Mix -60°C
No Matrix-M
HA (µg)
Matrix-M (µg)
6 3.6 6 3.6
5 3 5 3
1.5 0.9 1.5 0.9 1.5 0.9
5 3 5 3
High Dose
Low Dose

FIG. 25

12 months

Day 35 A/Brisbane Strain

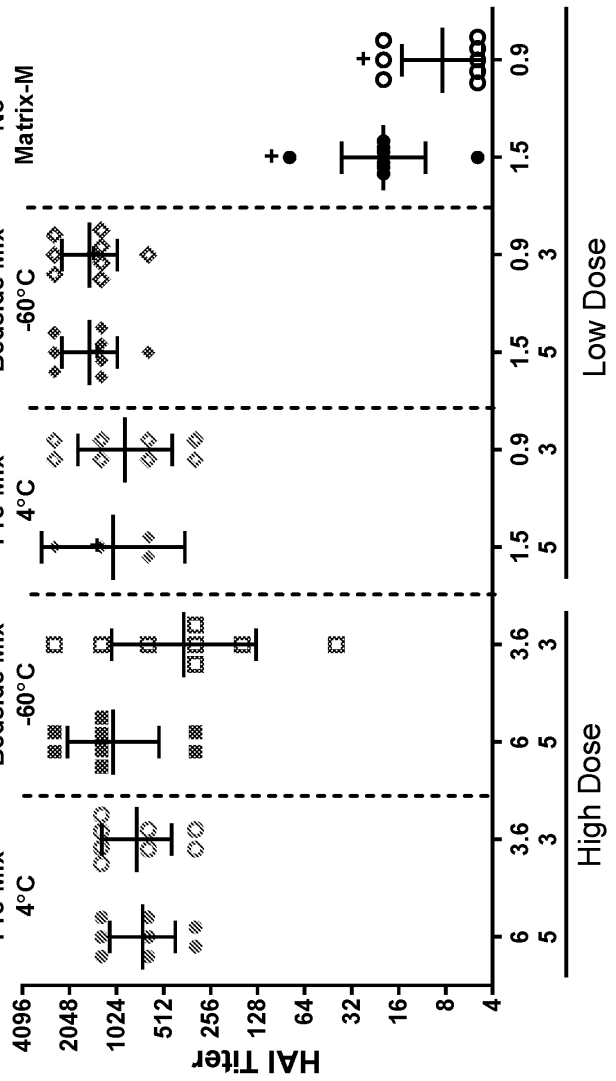


FIG. 26

12 months

Day 21 A/Phuket Strain

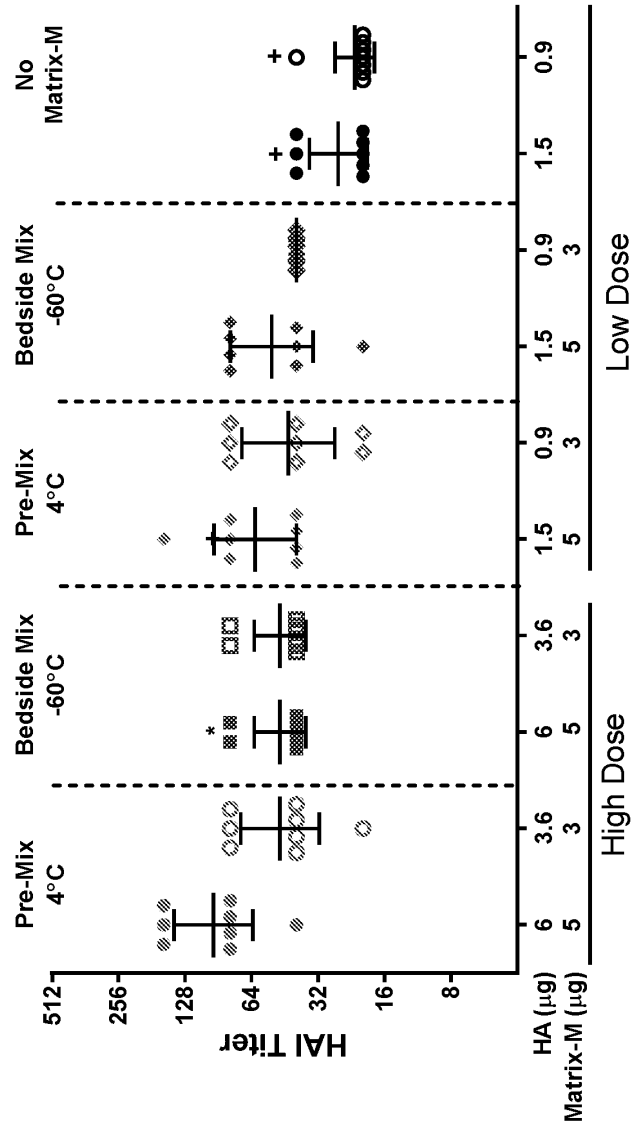


FIG. 27

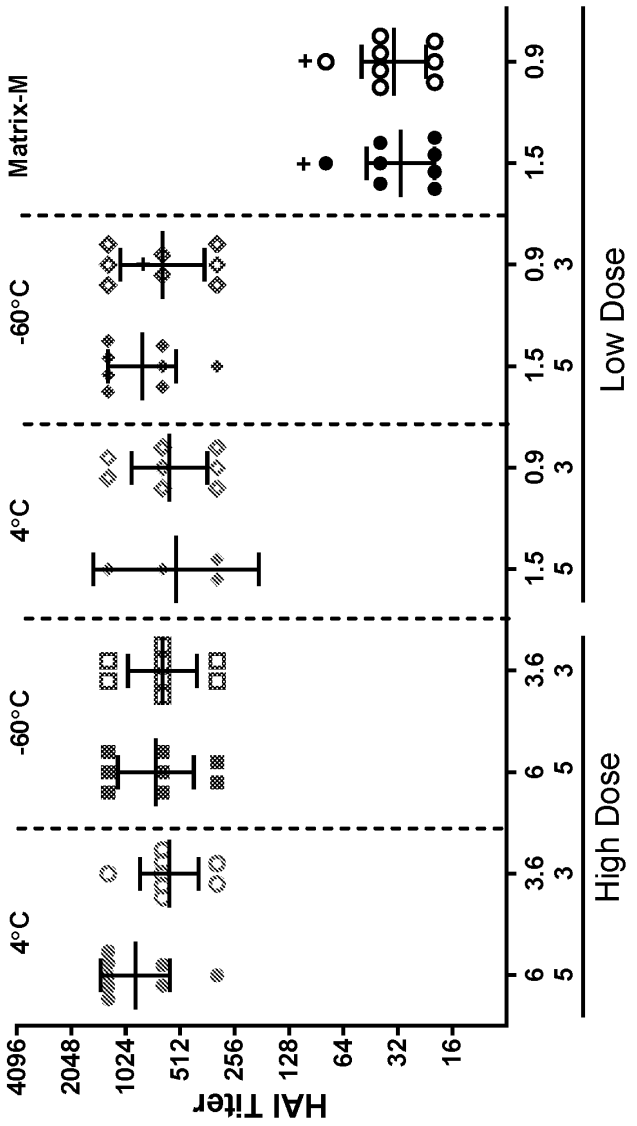

12 months
Day 35 A/Phuket Strain
HAI Titer
4096
2048
1024
512
256
128
64
32
16
Pre-Mix 4°C
Bedside Mix -60°C
Pre-Mix 4°C
Bedside Mix -60°C
No Matrix-M
6
5
3.6
3
6
5
3.6
3
1.5
5
0.9
3
1.5
5
0.9
3
1.5
0.9
High Dose
Low Dose

FIG. 28

Instrument	Value
Rotor speed	15000 rpm
Scans/sample	200
Detection	280 nm
US3	**Value**
S-Range	1-150 S
S-Grid	128 points
f/f0 Range	1-4
f/f0-Grid	64 points
V-bar, ū	0.7314
Density, ρ	1.03433
Viscosity, η	1.2398
Model	MC-50
smoothing	0.05 σ

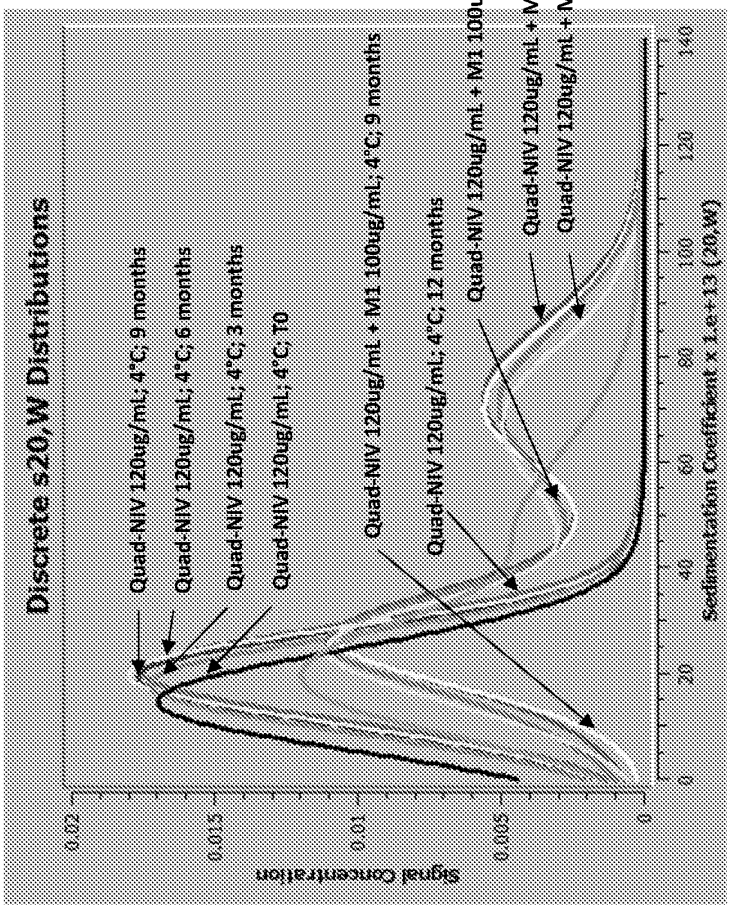
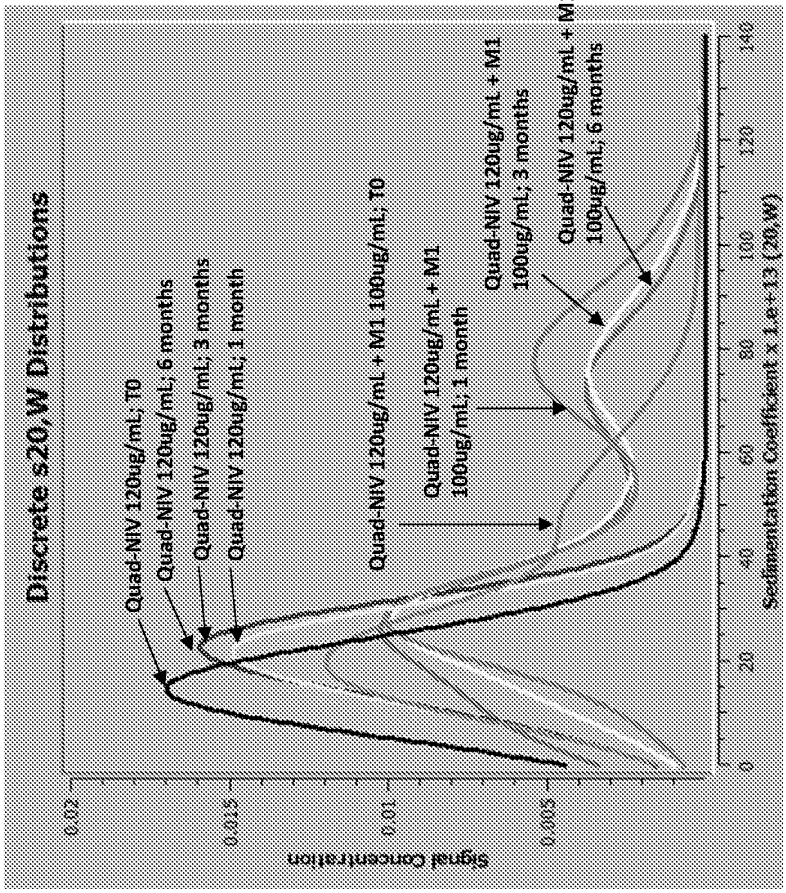


FIG. 29



Instrument	Value
Rotor speed	15000 rpm
Scans/sample	200
Detection	280 nm
UI3	**Value**
S-Range	1-150 S
S-Grid	128 points
f/f0 Range	1-4
f/f0-Grid	64 points
V-bar, ū	0.7314
Density, ρ	1.03433
Viscosity, η	1.2398
Model	MC-50
smoothing	0.05 σ

FIG. 30 HaSMaN formation at Time Zero

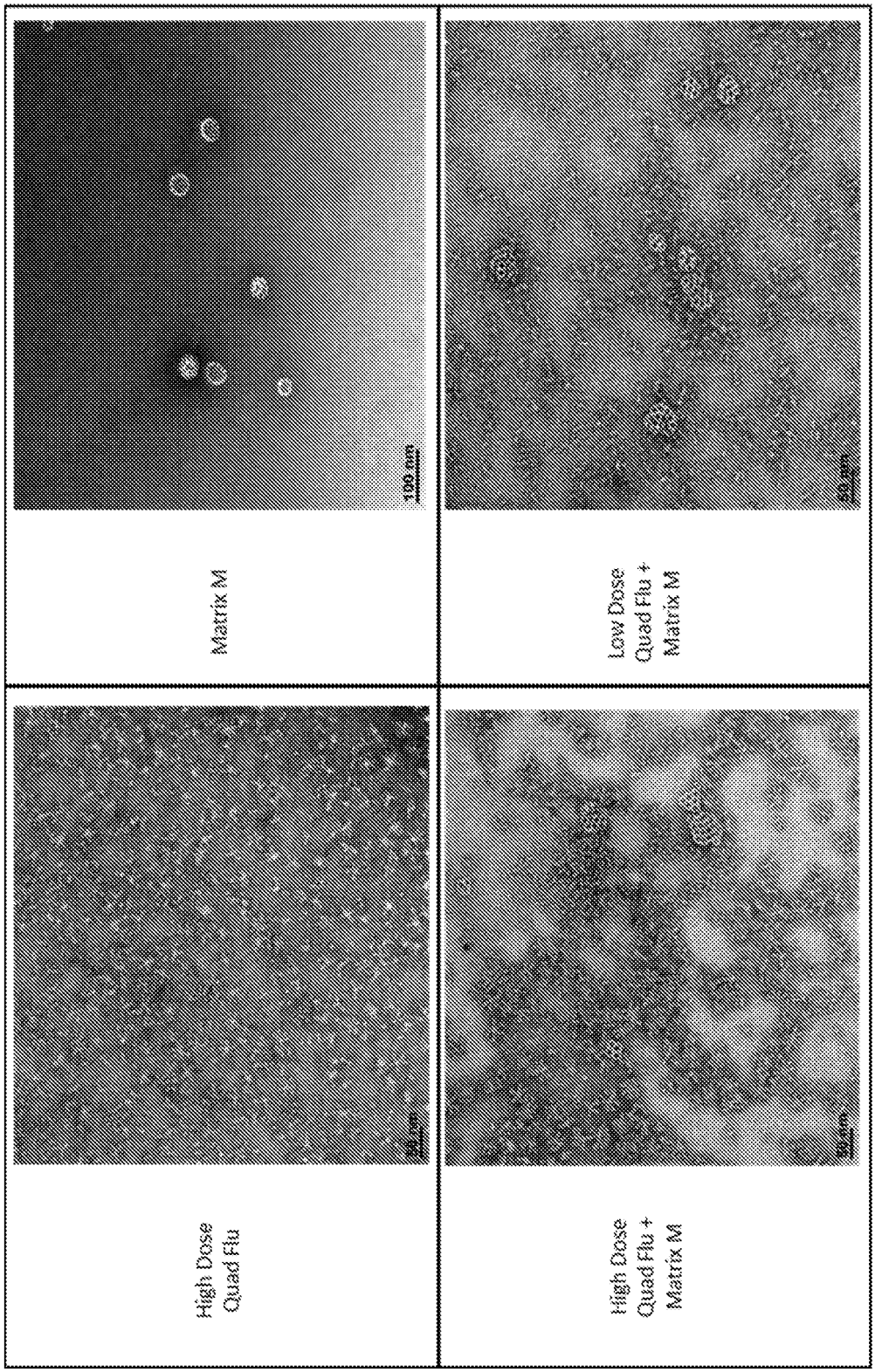


FIG. 31 HaSMaN formation at 4 hours

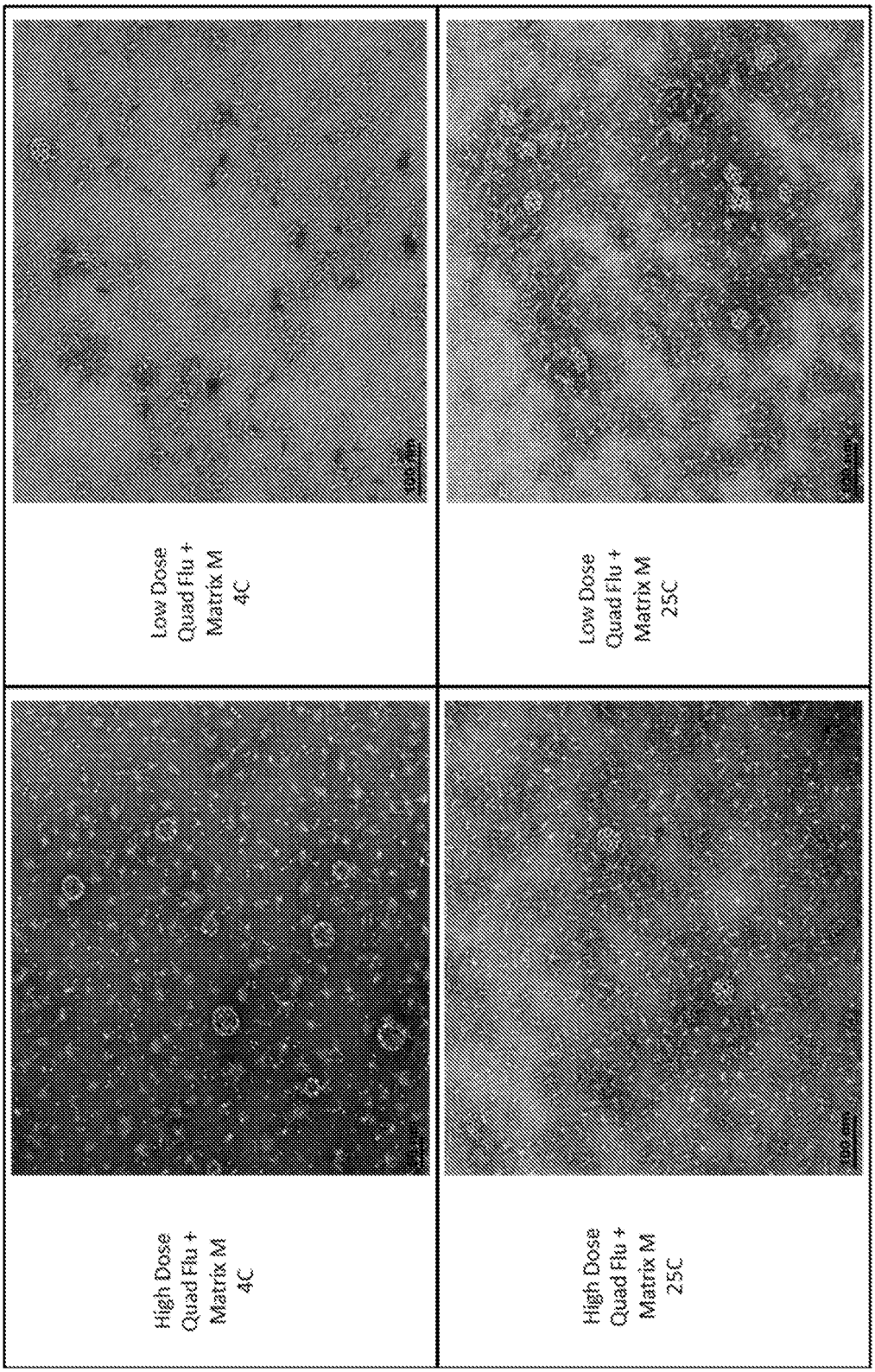


FIG. 32 HaSMaN formation at 24 hours

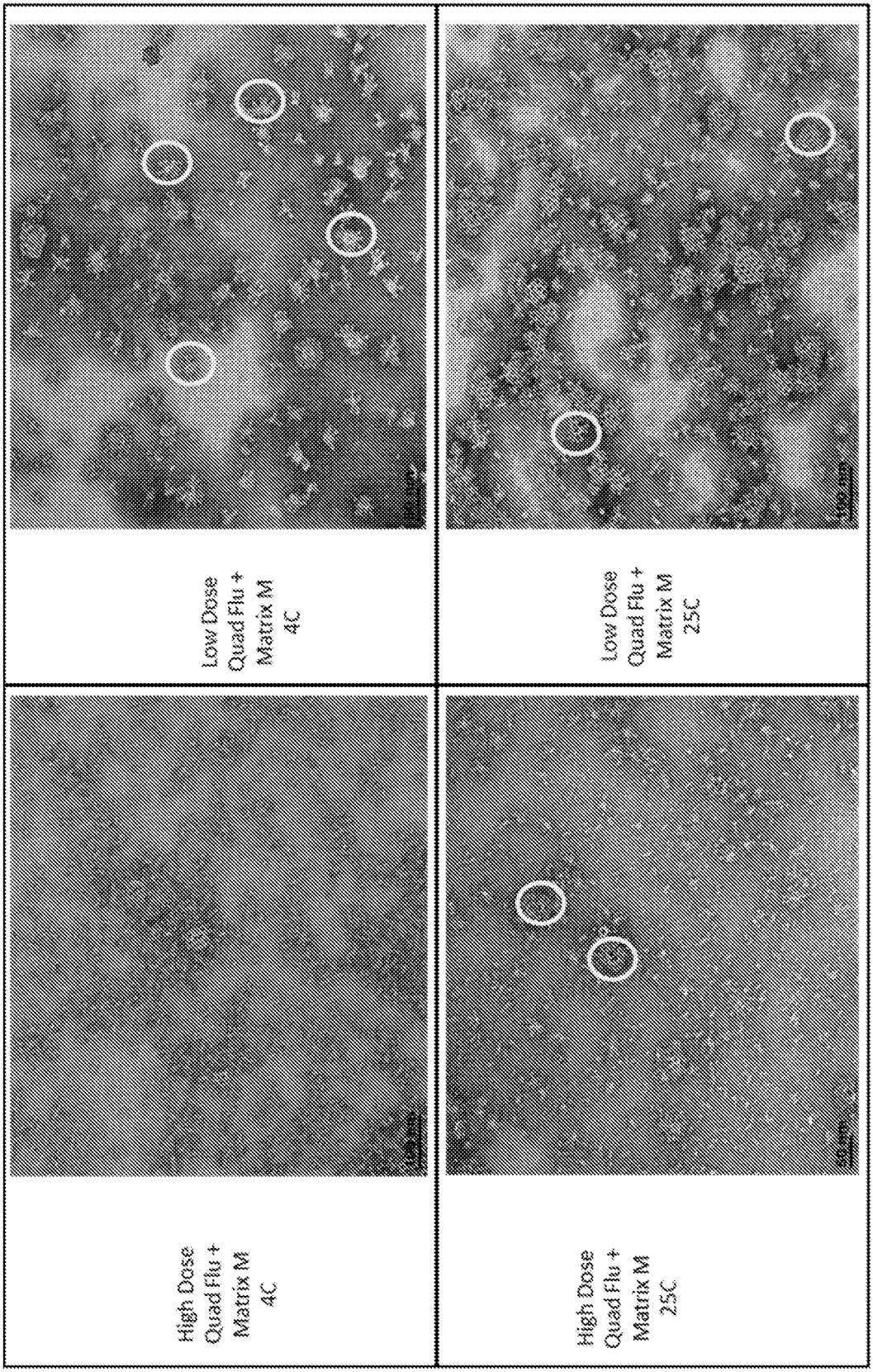


FIG. 33: HaSMaN formation at 48 hours

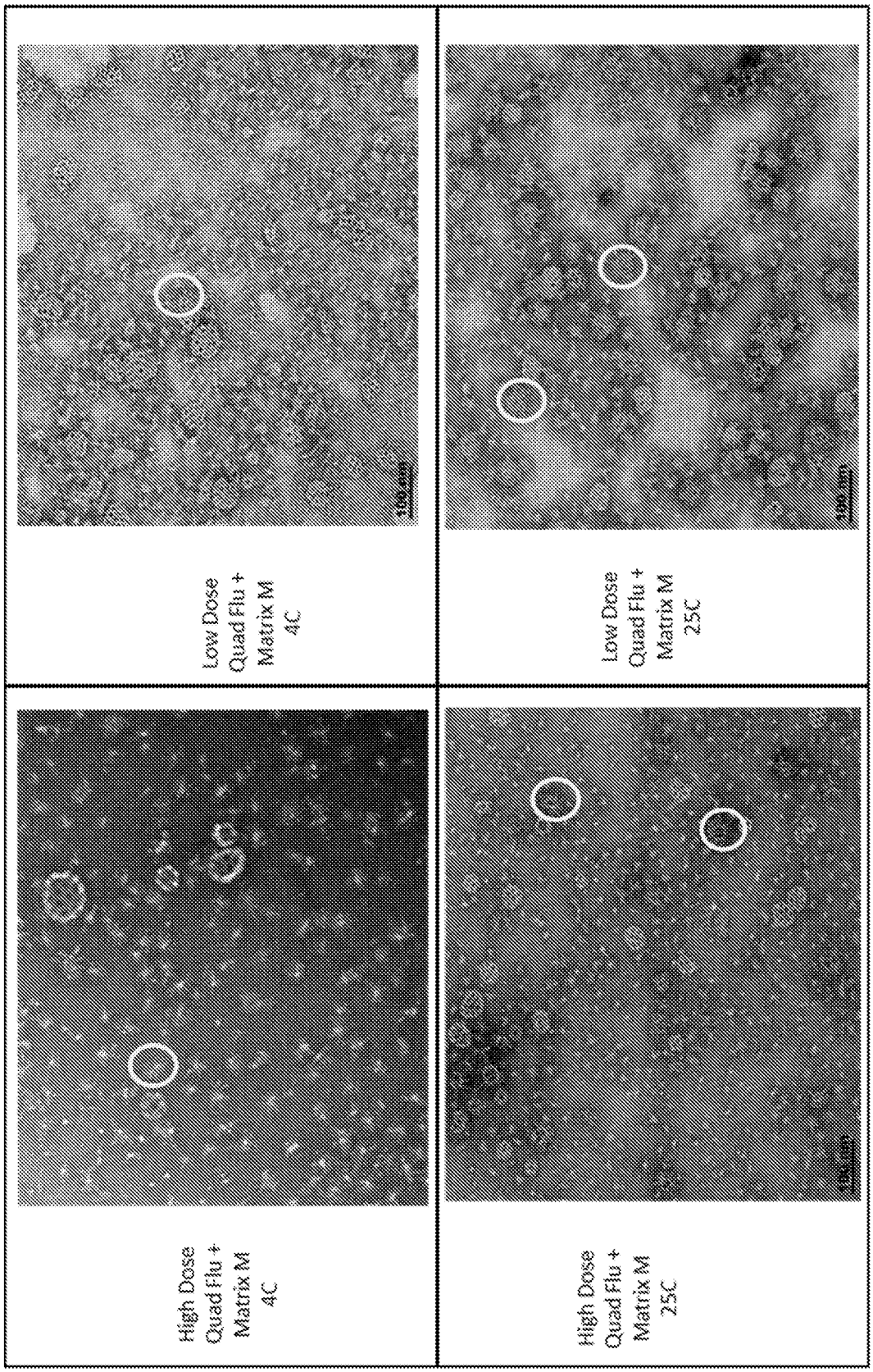


FIG. 34 HaSMaN formation at 7 days

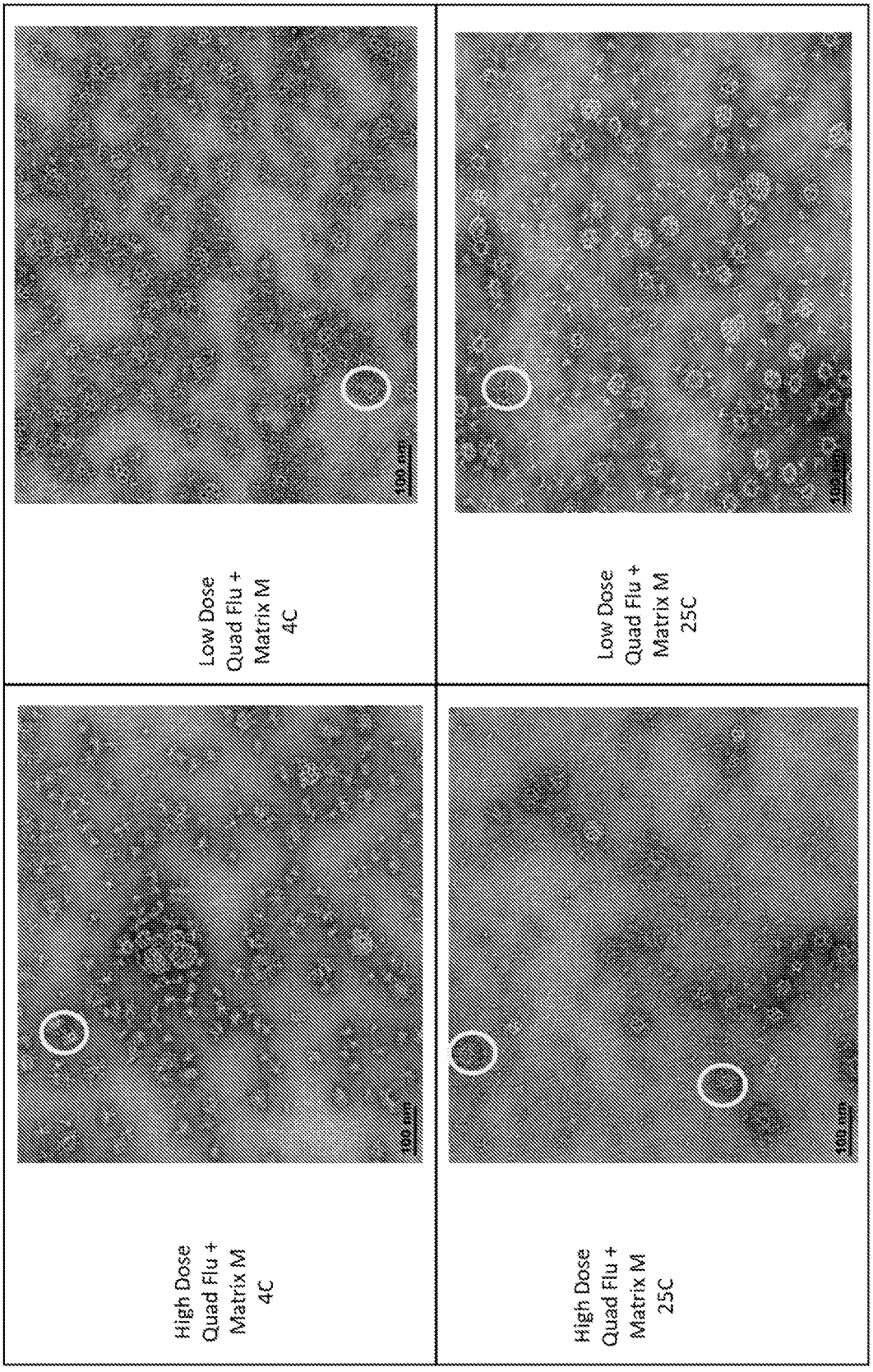


FIG. 35

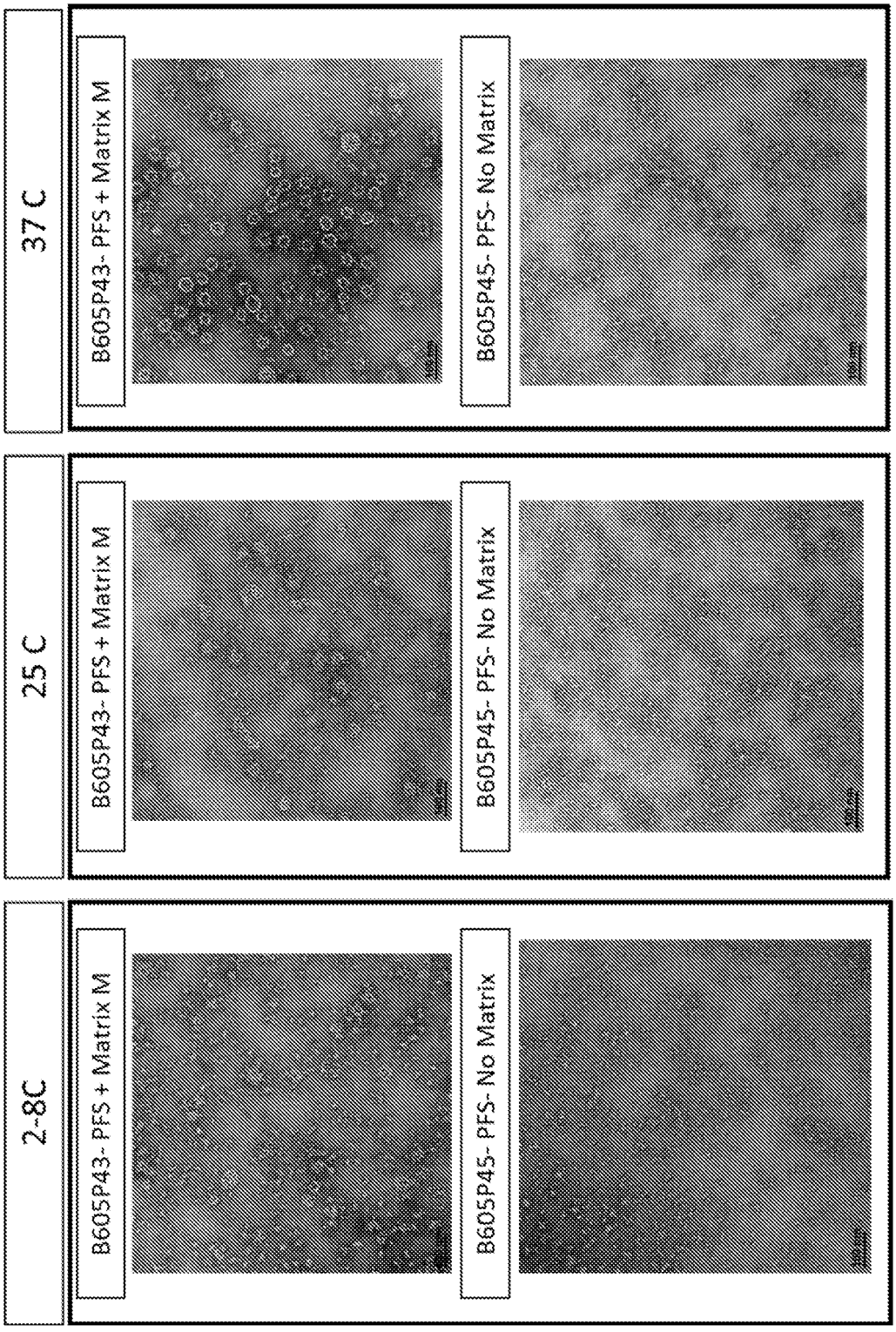

2-8C
B605P43- PFS + Matrix M
B605P45- PFS- No Matrix
25 C
B605P43- PFS + Matrix M
B605P45- PFS- No Matrix
37 C
B605P43- PFS + Matrix M
B605P45- PFS- No Matrix

FIG. 36

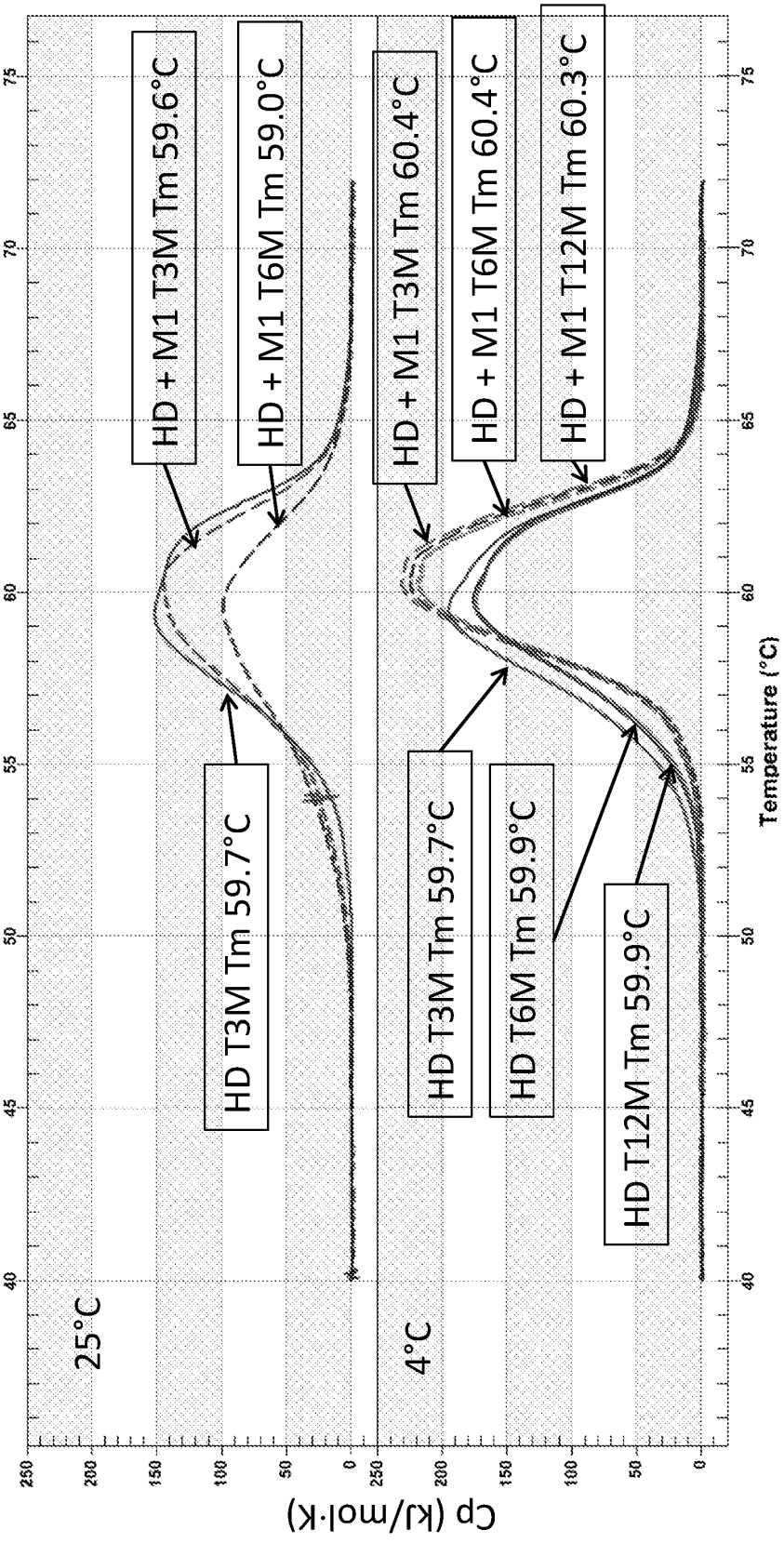

HD + M1 T3M Tm 59.6°C
HD + M1 T6M Tm 59.0°C
HD + M1 T3M Tm 60.4°C
HD + M1 T6M Tm 60.4°C
HD + M1 T12M Tm 60.3°C
HD T3M Tm 59.7°C
HD T3M Tm 59.7°C
HD T6M Tm 59.9°C
HD T12M Tm 59.9°C
25°C
4°C
Cp (kJ/mol·K)
Temperature (°C)

FIG. 37: Type A but not Type B strain HA glycoproteins form HaSMaNs

