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Process 2A: about 22 days from Steps A - E**1. STEP A**

Obtain Patient Tumor Sample

2. STEP B

Fragmentation and First Expansion

3 days to 14 days

3. STEP C

First Expansion to Second Expansion Transition

No Storage and Closed System

4. STEP D

Second Expansion

IL-2, OKT-3, and antigen-presenting feeder cells

Closed System

5. STEP E

Harvest TILS from Step D

Closed System

6. STEP F

Final Formulation and/or Transfer to Infusion Bag

(optionally cryopreserve)

Figure 1

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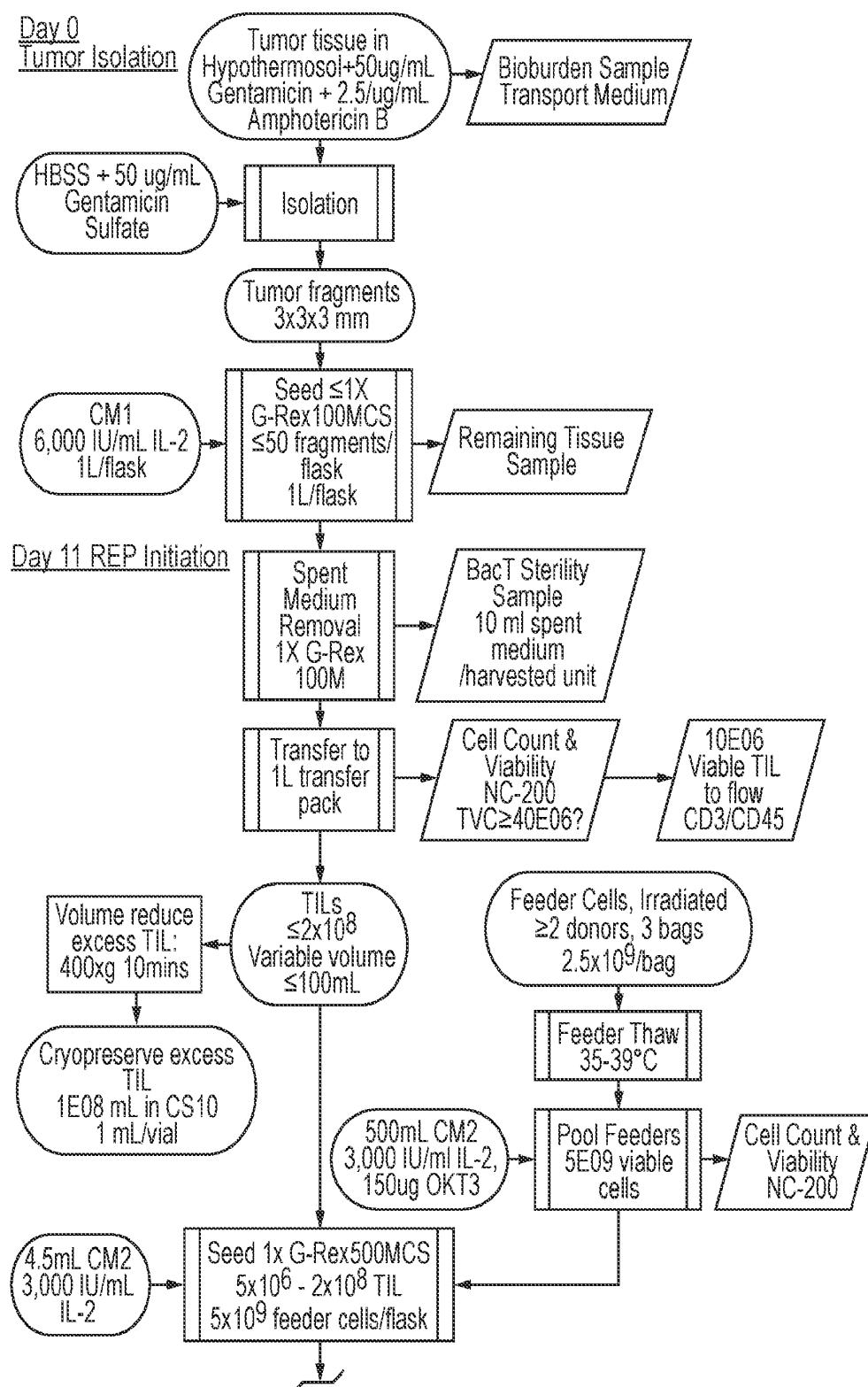


Figure 2B

Figure 2A

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Figure 2A

Day 16 - Culture Split

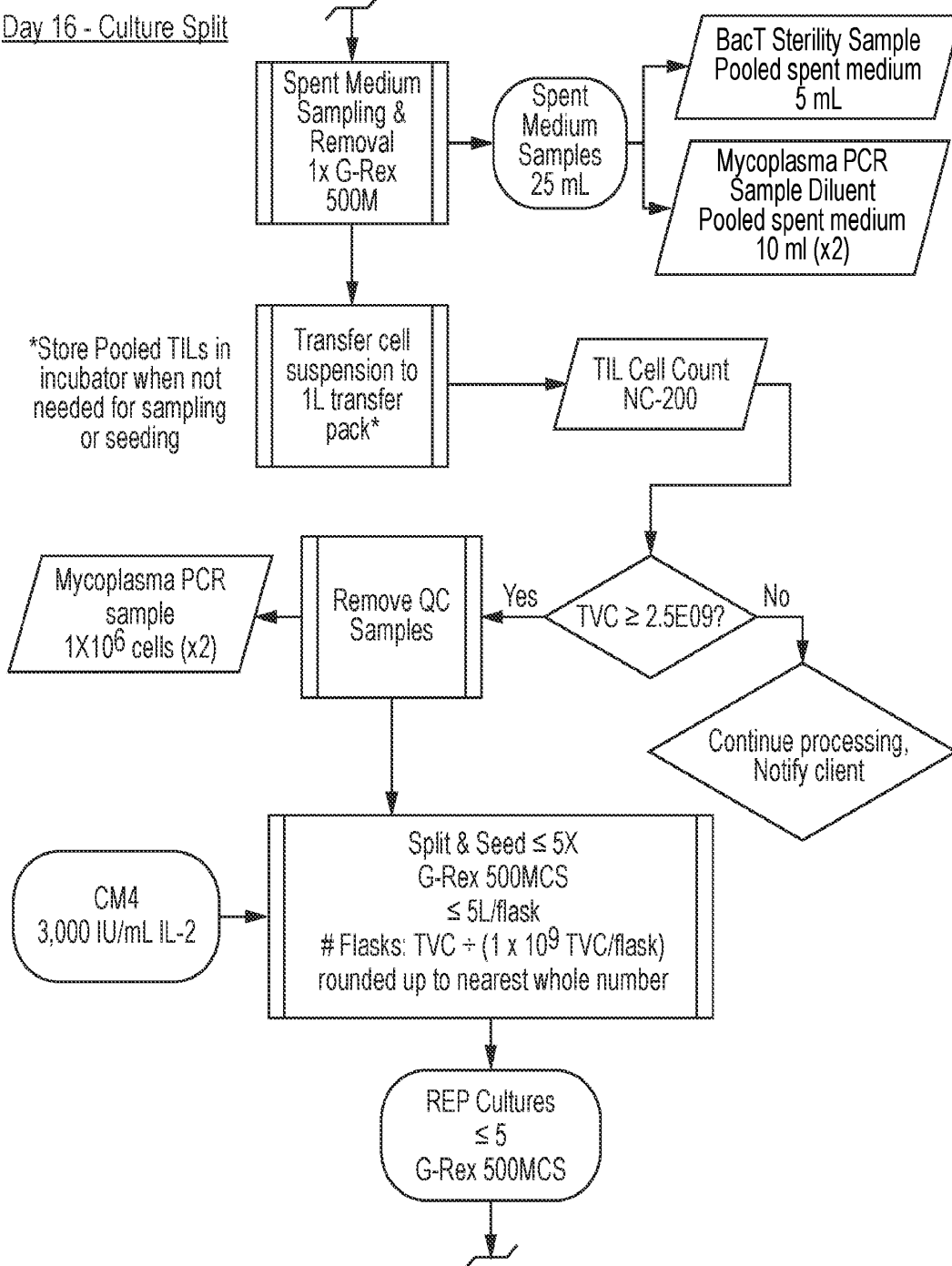


Figure 2C

Figure 2B

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Figure 2B

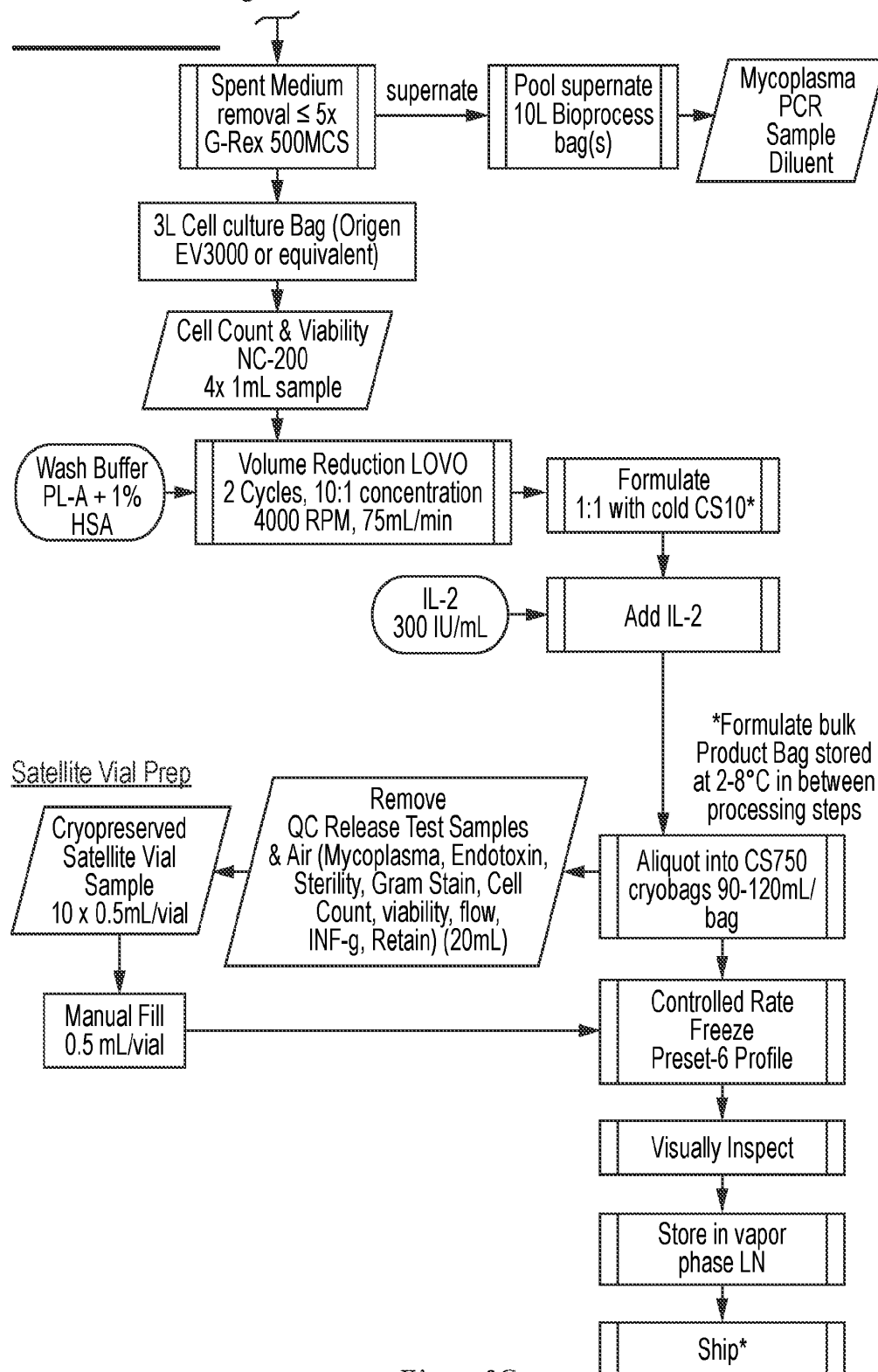


Figure 2C

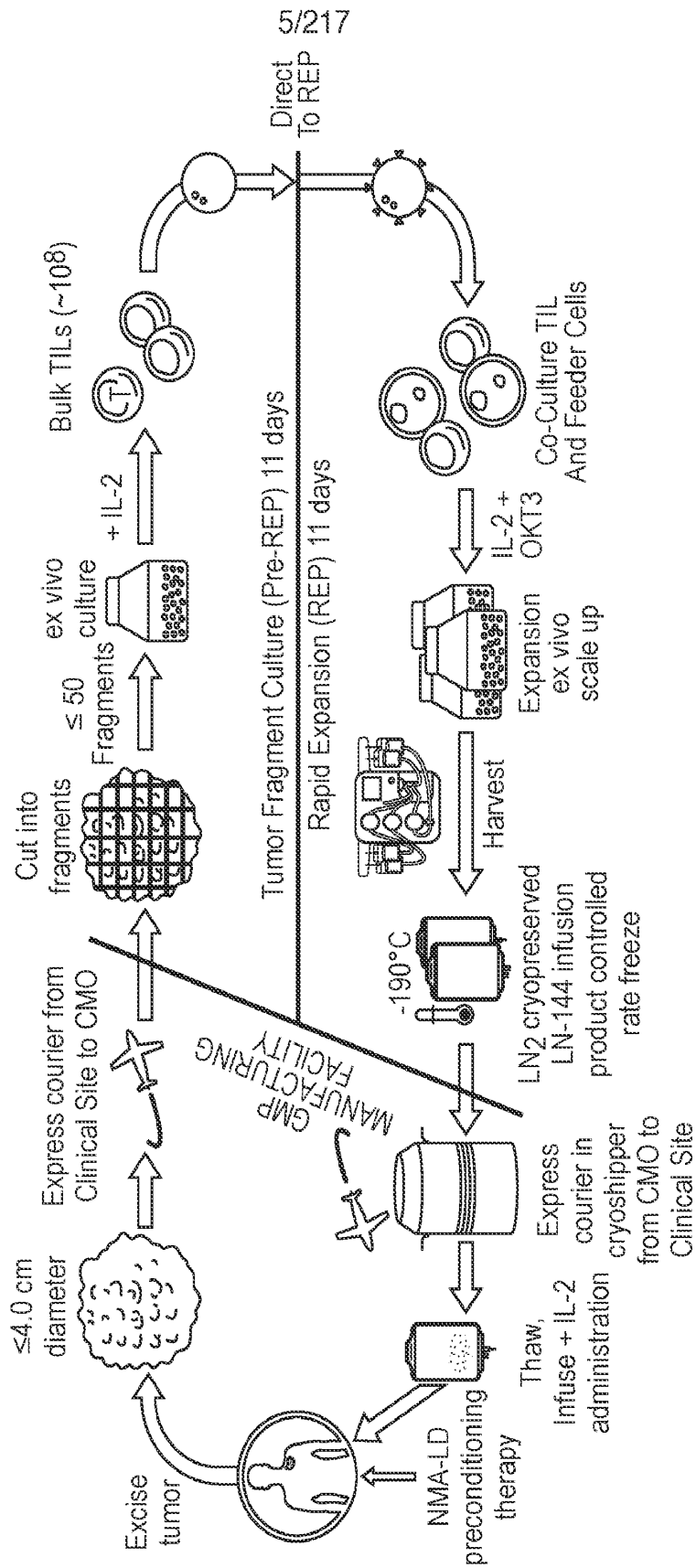


Figure 3

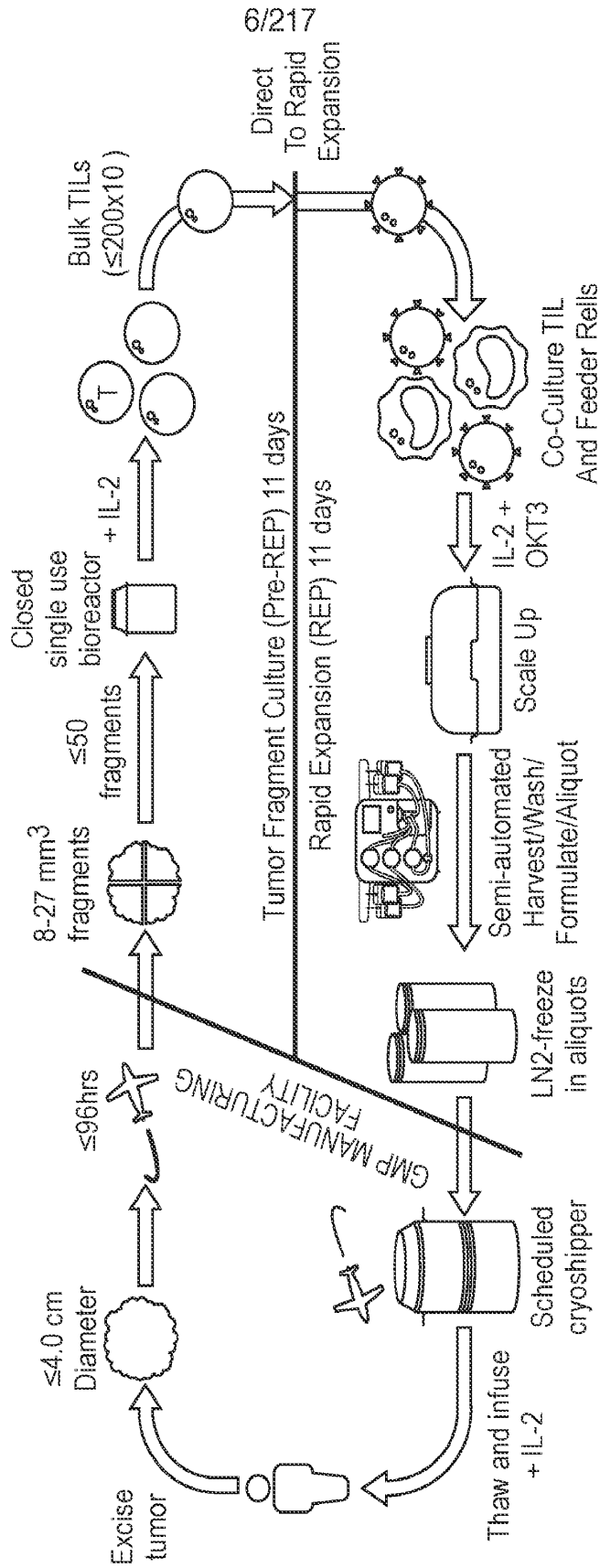


Figure 4

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Process 1C: 43-55 Days for Steps A - E	Process 2A: about 22 days from Steps A - E
1. <u>STEP A</u> Obtain Patient Tumor Sample	1. <u>STEP A</u> Obtain Patient Tumor Sample
2. <u>STEP B</u> Fragmentation and First Expansion 11 days to 21 days	2. <u>STEP B</u> Fragmentation and First Expansion 3 days to 14 days
3. <u>STEP C</u> First Expansion to Second Expansion Transition Optional Storage until Selection	3. <u>STEP C</u> First Expansion to Second Expansion Transition No Storage and Closed System
4. <u>STEP D</u> Second Expansion IL-2, OKT-3, antigen-presenting feeder cells Optionally repeat one or more times	4. <u>STEP D</u> Second Expansion IL-2, OKT-3, antigen-presenting feeder cells Closed System
5. <u>STEP E</u> Harvest TILs from Step D	5. <u>STEP E</u> Harvest TILs from Step D Closed System
6. <u>STEP F</u> Final Formulation and/or Transfer to Infusion Bag	6. <u>STEP F</u> Final Formulation and/or Transfer to Infusion Bag (optionally cryopreserve)

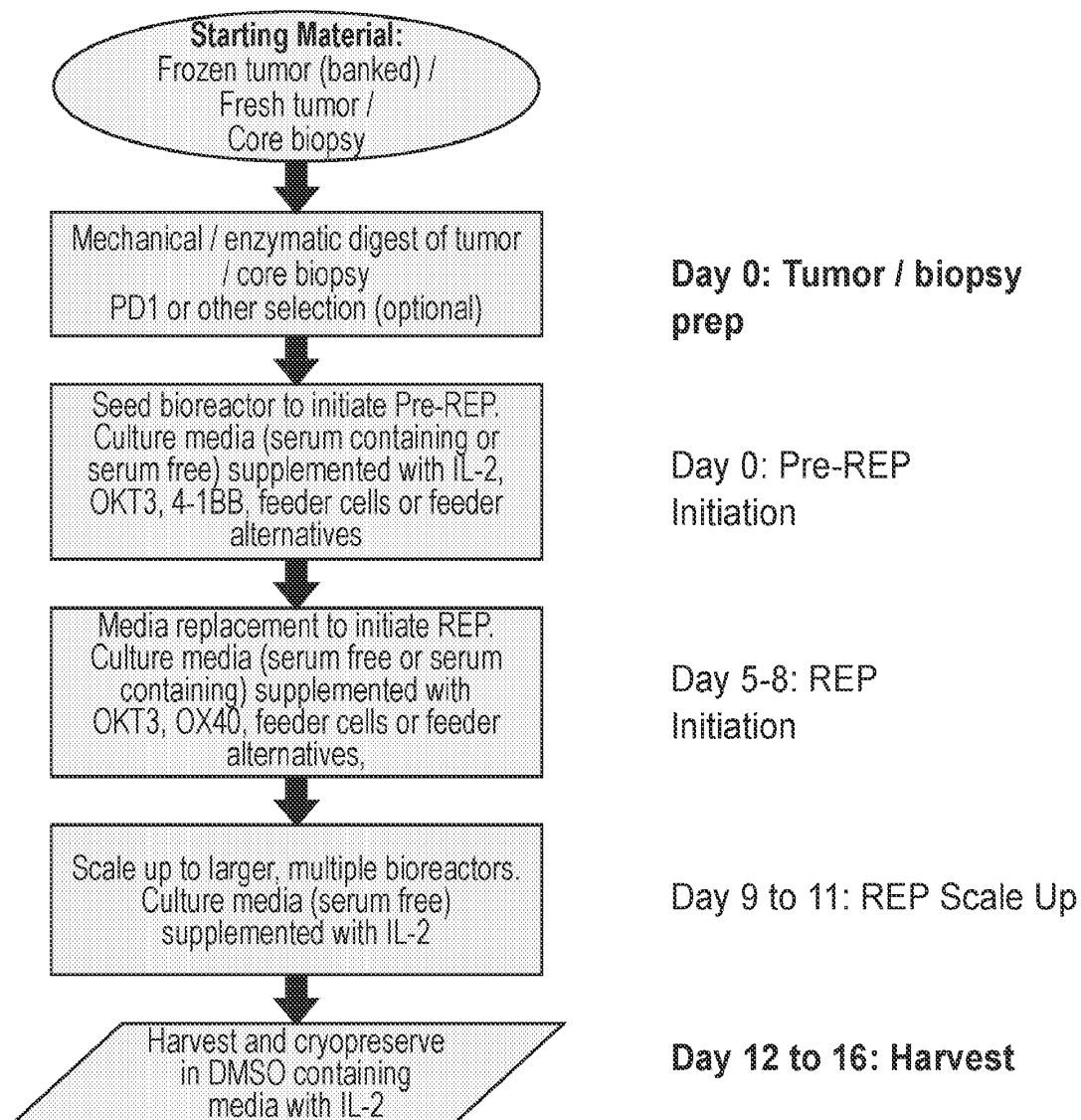
Figure 5

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Process Step	Process 1C Embodiment	Process 2A Embodiment	Advantages
Pre-REP	4 fragments per 10 GREX-10 flasks 11-21 day duration	40 fragments per 1 GREX-100M flask 11 day duration	- Increased tumor fragments per flask - Shortened culture time - Reduced number of steps - Amenable to closed system
Pre-REP to REP Transition	- Pre-REP TIL are frozen until phenotyped for selection then thawed to proceed to the REP (-day 30) - REP requires $>40 \times 10^6$ TIL	- Pre-REP TIL directly move to REP on day 11 - REP requires 25-200 $\times 10^6$ TIL	- Shortened pre-REP-to-REP process - Reduced number of steps - Eliminated phenotyping selection - Amenable to closed system
REP	6 GREX-100M flasks on REP day 0 5×10^6 TIL and 5×10^8 PBMC feeders per flask on REP day 0 - Split to 18-36 flasks on REP day 7 14 day duration	1 GREX-500M flask on day 11 25-200 $\times 10^6$ TIL and 5×10^9 PBMC feeders on day 11 - Split to ≤ 6 GREX-500M flasks on day 16 11 day duration	- Reduced number of steps - Shorter REP duration - Closed system transfer of TIL between flasks - Closed system media exchanges
Harvest	TIL harvested via centrifugation	TIL harvested via LOVO automated cell washing system	- Reduced number of steps - Automated cell washing - Closed system - Reduced loss of product during wash
Final Formulation	- Fresh product in Hypothermosol - Single infusion bag - Limited shipping stability	- Cryopreserved product in PlasmaLyte-A + 1% HSA and CS10 stored in LN₂ - Multiple aliquots - Longer shipping stability	- Shipping flexibility - Flexible patient scheduling - More timely release testing
Overall Estimated Process Time	43 -55 days	22 days	Faster turnaround to patient

Figure 6

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*Figure 7*

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Process 2A/Gen 2: about 22 days from Steps A -E Process Gen 3: about 14-18 days from Steps A -E

STEP A

Obtain Patient Tumor Sample
(optionally can be frozen before Step B)

STEP B

First Expansion
(physical fragmentation to at least 40 fragments per
container grown for about 3 days to 14 days with
media comprising IL-2)

STEP C

First Expansion to Second Expansion Transition
(Step B TILs directly move to Step D, optionally on
Step B day 11)

STEP D

Second Expansion
(TILs grown in growth media medium comprising
IL-2, OKT-3, and antigen-presenting feeder cells in a
closed container)

STEP E

Harvest TILs from Step D
(TILs harvested via closed system)

STEP F

Examine the potency and/or functionality of TIL s
from Step E

STEP G

Final Formulation and/or Transfer to Infusion Bag
(optionally cryopreserve)

STEP A

Obtain Patient Tumor Sample
(optionally can be frozen before Step B)

STEP B

Priming First Expansion
(physical fragmentation of up to 60 fragments per
container grown for about 1 days to 7 days with
media comprising IL-2, OKT-3, and antigen-
presenting feeder cells)

STEP C

Priming First Expansion to Rapid Second Expansion
Transition
(Step B TILs directly move to Step D on day 7)

STEP D

Rapid Second Expansion
(TILs grown in growth media medium comprising
IL-2, OKT-3, and 2X antigen-presenting feeder cells;
Days 10-11 scale up and add additional IL -2)

STEP E

Harvest TILs from Step D

STEP F

Examine the potency and/or functionality of TILs
from Step E

STEP G

Final Formulation and/or Transfer to Infusion Bag
(optionally cryopreserve)

Figure 8A

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Process Gen 3: about 14-18 days from Steps A-E**STEP A**

Obtain Patient Tumor Sample
(optionally can be frozen before Step B)

STEP B

Priming First Expansion
(physical fragmentation of up to 60 fragments per container grown for about 1 days to 7 days with media comprising IL-2, OKT-3, and antigen-presenting feeder cells)

STEP C

Priming First Expansion to Rapid Second Expansion Transition
(Step B TILs directly move to Step D on day 7)

STEP D

Rapid Second Expansion
(TILs grown in growth media medium comprising IL-2, OKT-3, and 2X antigen-presenting feeder cells; Days 10-11 scale up and add additional IL-2)

STEP E

Harvest TILS from Step D

STEP F

Examine the potency and/or functionality of TILs from Step E

STEP G

Final Formulation and/or Transfer to Infusion Bag
(optionally cryopreserve)

Figure 8B

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Embodiment Gen 3.0: about 14-18 days from Steps A - E	Embodiment Gen 3.1 control: about 14-18 days from Steps A - E	Embodiment Gen 3.1 Test/F: about 14-18 days from Steps A - E
<u>STEP A</u> Obtain Patient Tumor Sample (optionally can be frozen before Step B)	<u>STEP A</u> Obtain Patient Tumor Sample (optionally can be frozen before Step B)	<u>STEP A</u> Obtain Patient Tumor Sample (optionally can be frozen before Step B)
<u>STEP B</u> Priming First Expansion (physical fragmentation of up to 60 fragments per container grown for about 1 days to 7/8 days with media comprising IL-2)	<u>STEP B</u> Priming First Expansion (physical fragmentation of up to 60 fragments per container grown for about 1 days to 7/8 days with media comprising IL-2, and OKT-3)	<u>STEP B</u> Priming First Expansion (physical fragmentation of up to 60 fragments per container grown for about 1 days to 7/8 days with media comprising IL-2, OKT-3, and antigen- presenting feeder cells)
<u>STEP C</u> Priming First Expansion to Rapid Second Expansion Transition (Step B TILs directly move to Step D on day 7/8)	<u>STEP C</u> Priming First Expansion to Rapid Second Expansion Transition (Step B TILs directly move to Step D on day 7/8)	<u>STEP C</u> Priming First Expansion to Rapid Second Expansion Transition (Step B TILs directly move to Step D on day 7/8)
<u>STEP D</u> Rapid Second Expansion (TILs grown in growth media medium comprising IL-2, OKT-3, and antigen-presenting feeder cells; Days 10-11 scale up and add additional IL-2)	<u>STEP D</u> Rapid Second Expansion (TILs grown in growth media medium comprising IL-2, OKT-3, and 2X antigen- presenting feeder cells; Days 10-11 scale up and add additional IL-2)	<u>STEP D</u> Rapid Second Expansion (TILs grown in growth media medium comprising IL-2, OKT-3, and 2X antigen-presenting feeder cells; Days 10-11 scale up and add additional IL-2)
<u>STEP E</u> Harvest TILs from Step D	<u>STEP E</u> Harvest TILs from Step D	<u>STEP E</u> Harvest TILs from Step D
<u>STEP F</u> Examine the potency and/or functionality of TILs from Step E	<u>STEP F</u> Examine the potency and/or functionality of TILs from Step E	<u>STEP F</u> Examine the potency and/or functionality of TILs from Step E
<u>STEP G</u> Final Formulation and/or Transfer to Infusion Bag (optionally cryopreserve)	<u>STEP G</u> Final Formulation and/or Transfer to Infusion Bag (optionally cryopreserve)	<u>STEP G</u> Final Formulation and/or Transfer to Infusion Bag (optionally cryopreserve)

Figure 8C

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Modified Gen 2-like Process: about 22 days from Steps A - E**STEP A**

Obtain Patient Tumor Sample
(optionally can be frozen before Step B;
optionally tumor sample can be a core/small biopsy)

STEP B1

Initial Culture
physical fragmentation of up to 60 tumor fragments or up to 10 cores/small biopsies
per container, TILs grown for 3 days in growth medium comprising IL-2

STEP B2

Priming First Expansion
TILs grown for 8 days in growth medium comprising IL-2, OKT-3, and antigen-presenting feeder cells)

STEP C

Priming First Expansion to Rapid Second Expansion Transition
(Step B TILs directly move to Step D on day 11)

STEP D

Rapid Second Expansion
(volume reduced; TILs grown in growth media medium comprising IL-2, OKT-3, and
50X antigen-presenting feeder cells; Day 16 scale up and add additional IL-2)

STEP E

Harvest TILS from Step D

STEP F

Examine the potency and/or functionality of TILs from Step E

STEP G

Final Formulation and/or Transfer to Infusion Bag
(optionally cryopreserve)

Figure 8D

SUBSTITUTE SHEET (RULE 26)

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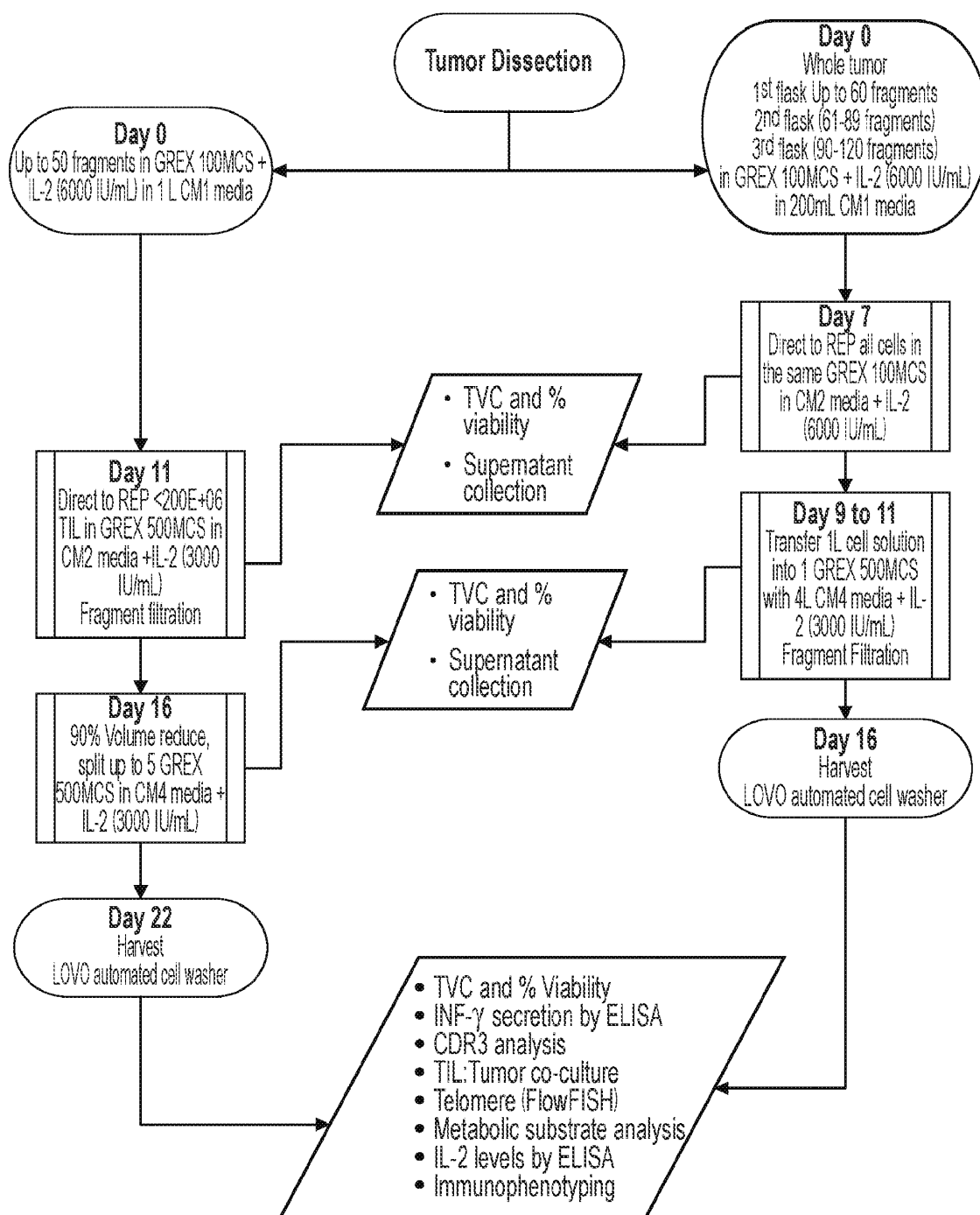


Figure 9

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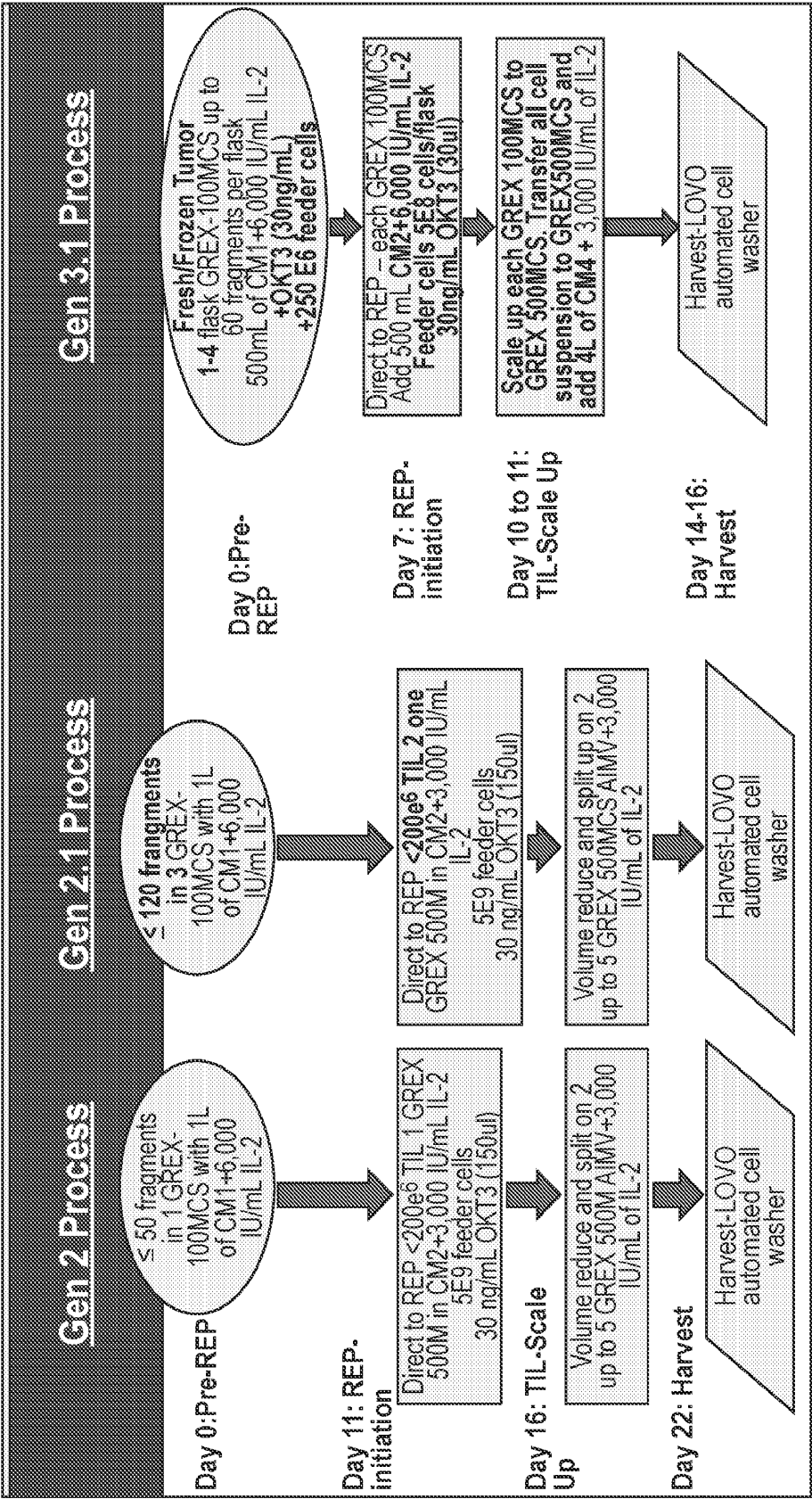


Figure 10

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STEP	Gen 2	Gen 2.1	Gen 3.0 Optimized
Pre REP- day 0	≤ 50 fragments/ 1 G-Rex 100MCS - 11 days	≤ 180 fragments/ 3 G-Rex, Pre-formulated CM1 warmed media 100MCS - 11 days	Fresh or Frozen Tumor Whole tumor with ≤ 30 fragments up to 60 fragments per 1 G-Rex. 100MCS (up to 4 G-Rex), preformulated warmed media - 7 days. Pre REP, Feeders 2.5 E8 cells + OKT-3 (30ng/mL)
REP Initiation	Direct to REP - Day 11- <200 E6 TIL 1 G-Rex 500MCS	Direct to REP - Day 11- <200 E6 TIL Pre-formulated CM2 warmed media in one G-Rex 500MCS	Direct to REP - Day 7-all cells TIL- same G-Rex 100MCS (100MCS up to 4 GREX), Standard media or Defined Media (Serum free). Addition Feeders 5 E8 cells +OKT-3 (30ng/mL)
TIL propagation or Scale up	1 to 5 G-REX 500MCS Split day 16	2 to 5 G-REX 500MCS Pre-formulated CM4 warmed media Split day 16	From G-REX 100MCS transfer TIL suspension to G- REX 500MCS, up to 4 GREX 500 MCS- Standard media or Defined Media (Serum Free) Scale up on day 10 or 11
Harvest	Harvest day 22, LOVO-automated cell washer	Harvest day 22, LOVO-automated cell washer (5 wash cycle)	Harvest day 14 or 16 LOVO- automated cell washer (5 wash cycle)
Final formulation	Cryopreserved Product 300IU/ml IL2- CS10 in LN ₂ , multiple aliquots	Cryopreserved Product 300IU/ml IL2- CS10 in LN ₂ , multiple aliquots	Cryopreserved product 300IU/ml IL-2- CS10 in LN ₂ , multiple aliquots
Process time	22 days	22 days	16 days

Figure 11

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Process Day	Conditions	Gen 3.1
Day 0- pre REP initiation	Media CM1	500 mL
	IL-2 (6000 IU/mL)	+
	OKT-3 (30ng/mL)	+
	Feeders (250 E+06)	+
Process Day	Conditions	Gen 3.1
Day 7- REP initiation	Media CM2	500 mL
	IL-2 (6000 IU/mL)	+
	OKT-3 (30ng/mL) added on Day 7	+
	Feeders Added on Day 7	500 E06
	Total Feeders at Day	750 E+06
Process Day	Conditions	Gen 3.1
Day 9-11 - Scale Up	From G-REX 100MCS transfer TIL suspension to 1 G-REX 500MCS (up to 3 GREX 500MCS)	Yes
Day 16 - Harvest	LOVO- automated cell washer	Yes

Figure 12

Process Comparison	Key Process Changes	Benefit
Gen 2 : Gen 2.1	• Initiate process with two flasks instead of one flask • Divide REP initiation feeder layer between 2 G-Rex500MCS Flasks • Pre-formulate media and warm prior to use	• Potential doubling of final cell count (dose) with increased TIL repertoire. • Process redundancy throughout process
Gen 2.1 : Gen 3.1	• Fresh or Frozen tumor • 14-16 day process (from 22 day) • Reduce total feeder layer on process • Feeder layer and OKT3 present at Day 0 • REP initiated with fragments • 100MCS scales to 500MCS • Scales to multiple pre-REP flasks • Standard Media and Defined Media (Serum Free)	• Increased potency • Improved phenotype • Decreased process time • Reduced reagent testing • Decreased process variability • Defined reagents • Increased repertoire • Reduce impurities (feeder) • Comparable or Higher Dose.

Figure 13

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Process Comparison	Key Process Changes	Desired Improvement	Criteria for Success	Outcome
Gen 2 : Gen 3.0	• 14-16 days • Initiate REP with fragments up to 4 flask. • 100MCS scales to 500MCS	• Increased potency • Improved phenotype • Decreased process time	• Increase potency as measured by INF-g ✓ • Comparable phenotype ✓ • Comparable Dose ✓ • Comparable purity (feeder cell) ✓ • Maintain clonal diversity ✓	• Potency increased over Gen2 • Improved expression of CD28 on CD8 cells • Maximum capacity of flask reached by day 16 on Gen 3.1 • Reduced feeder cell usage • Increased diversity

Figure 14

Process	Gen 3	Gen 3.1 control	Gen 3.1
L4063	Standard Media	Standard Media	Standard Media
L4064	Defined Media	Defined Media	Defined Media

Defined Media:
CTS Optimizer (Serum Free Media) in each day of the process

Figure 15

Process	Gen 2	Gen 3
L4054	Standard Media	Standard Media
L4055	Standard Media	Standard Media
M1085T	Standard Media	Standard Media

Standard Media:
Pre REP: CM1
REP initiation : CM2
Split or Scale up : CM4

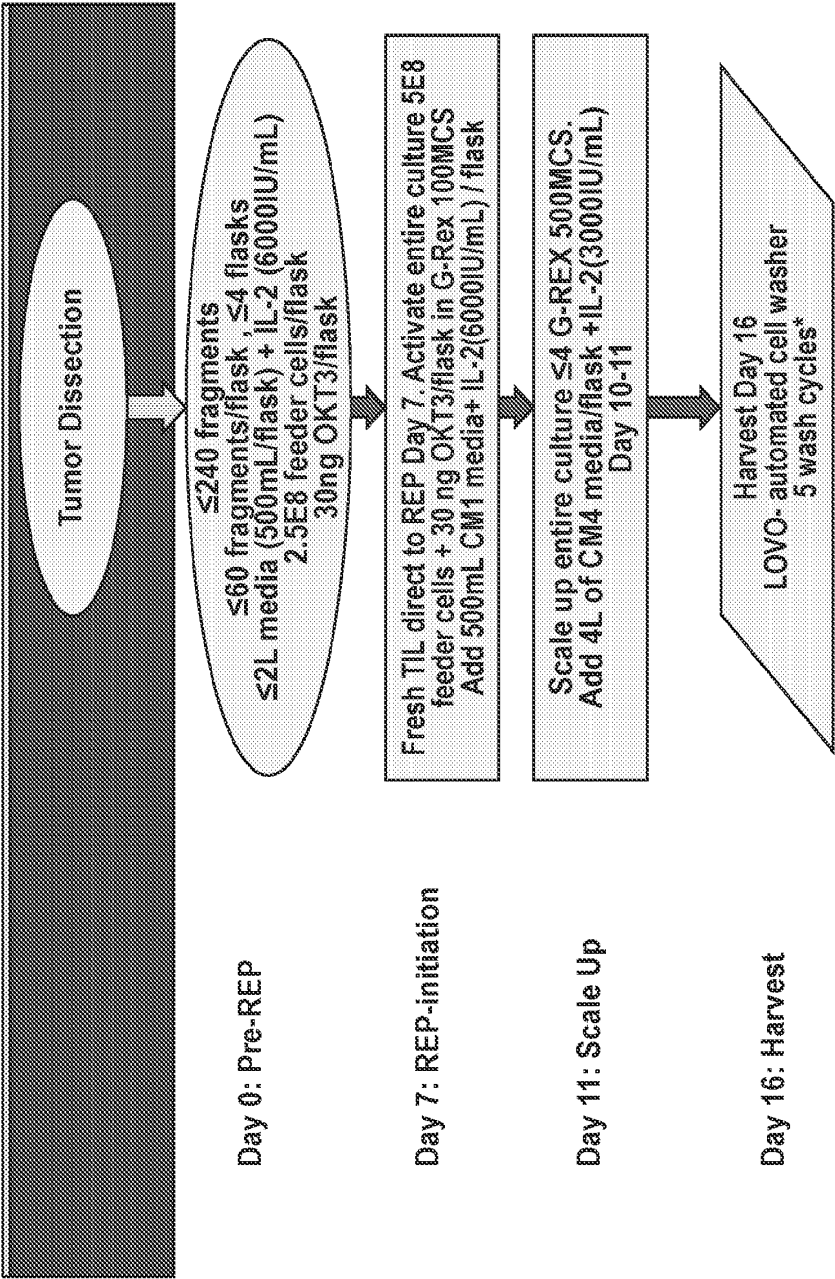
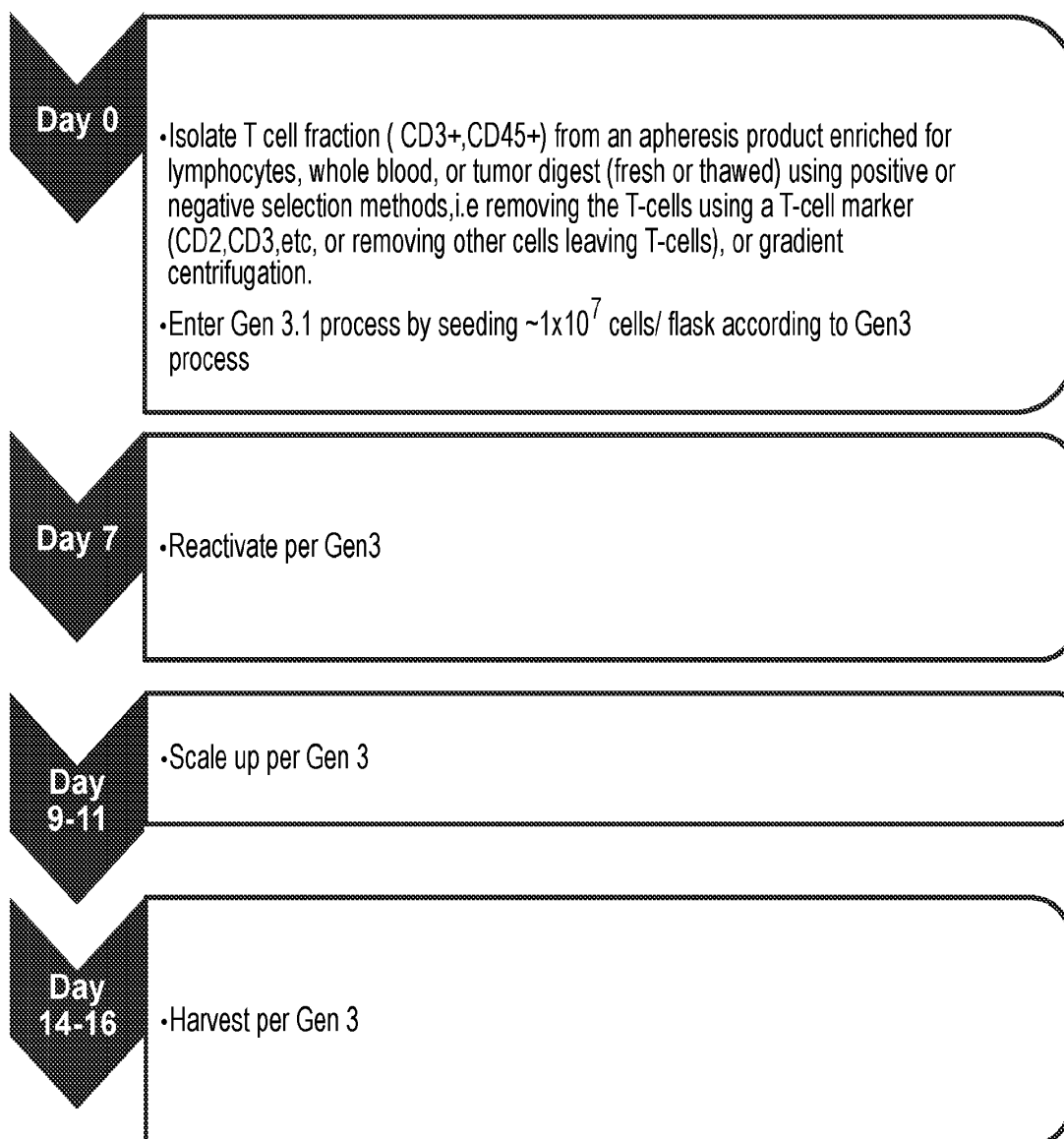
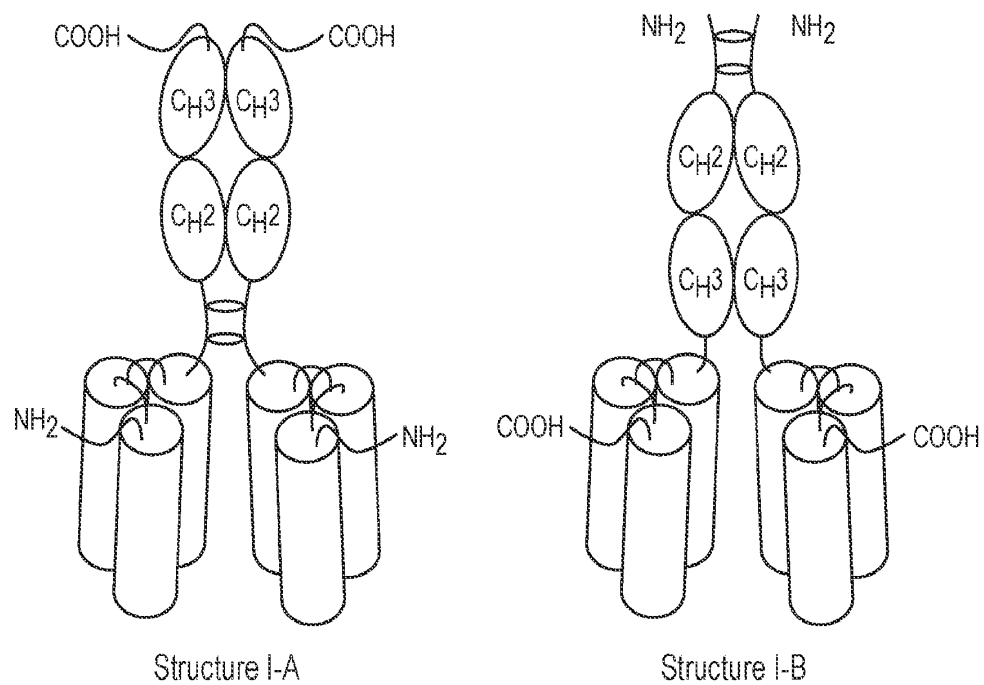


Figure 16

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*Figure 17*

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*Figure 18*

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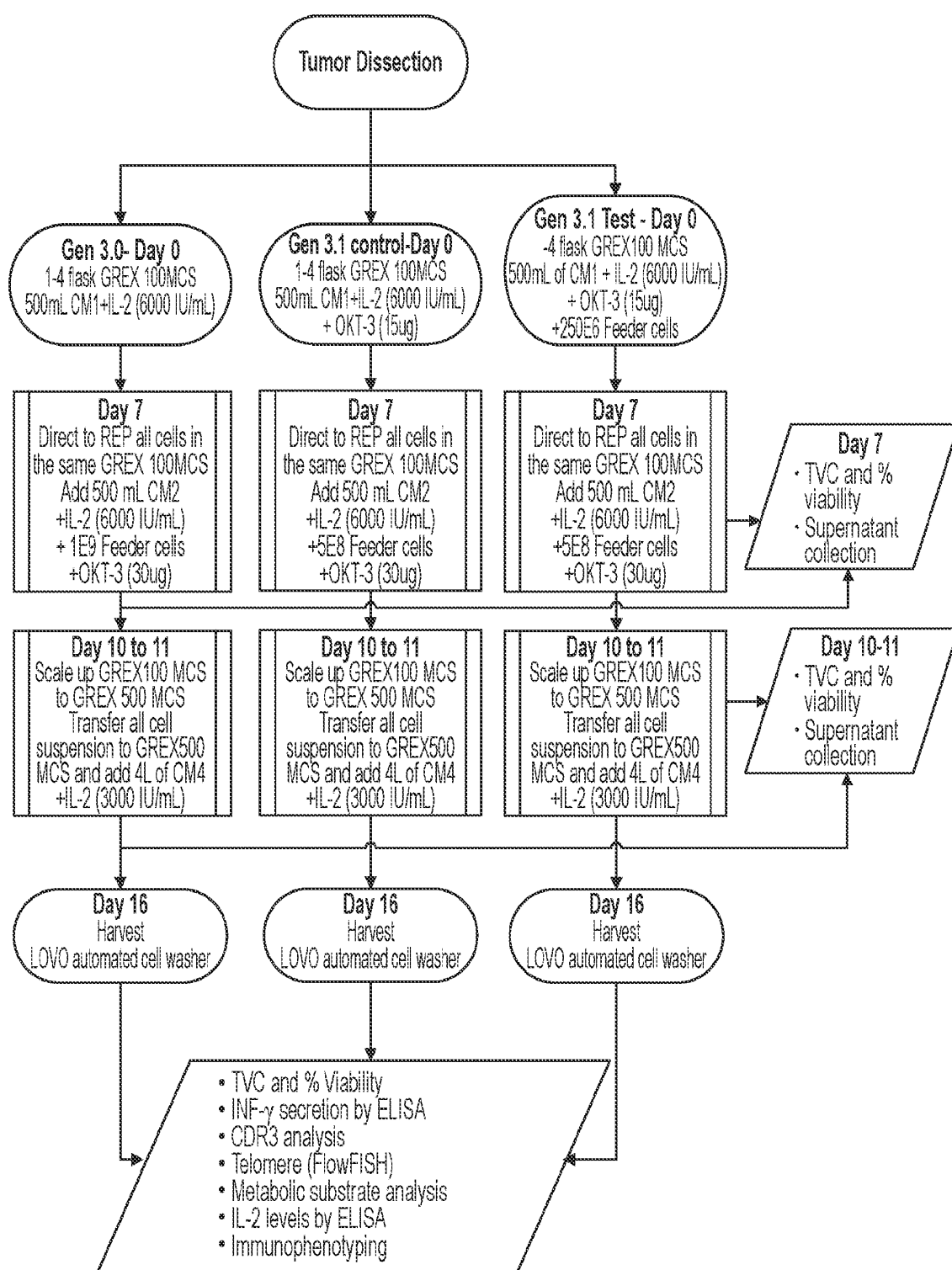


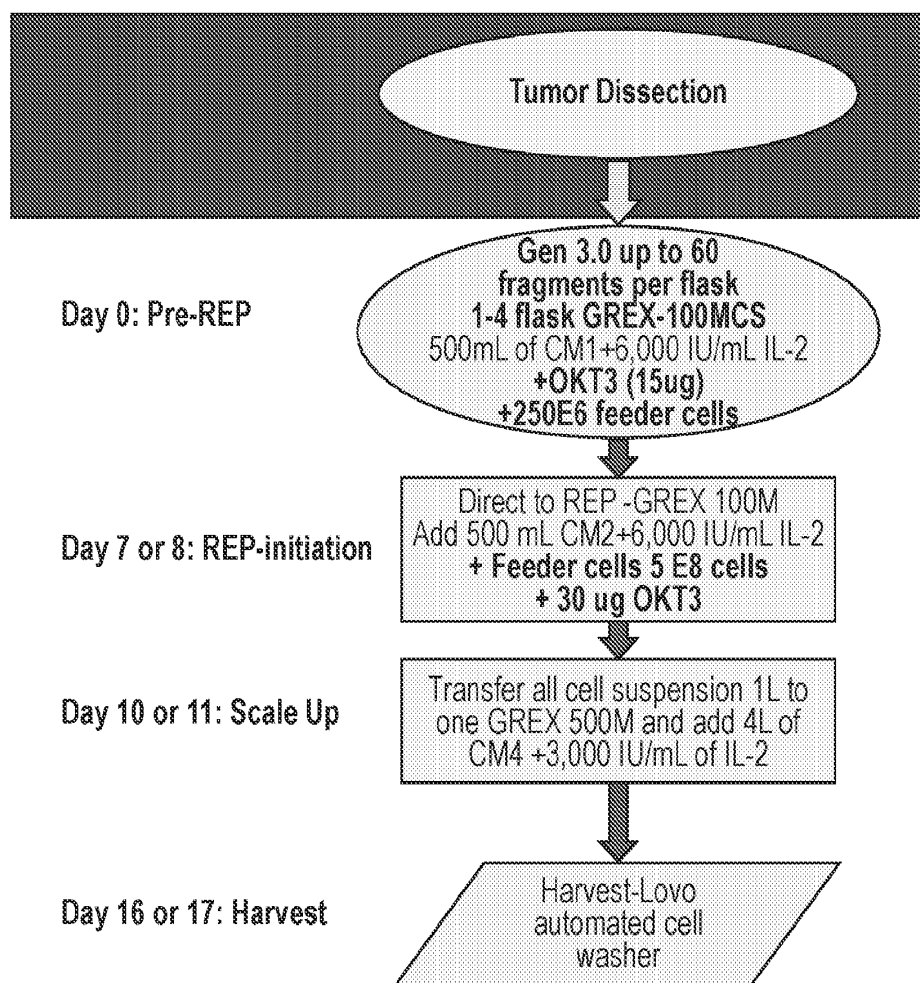
Figure 19

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Process Day	Conditions	Gen 3.1 Test
Day 0- pre REP initiation	Media CM1	500 mL
	IL-2 (6000 IU/mL)	+
	OKT-3 (15ug)	+
	Feeders (250 E+06)	+
Process Day	Conditions	Gen 3.1 Test
Day 7- REP initiation	Media CM2	500 mL
	IL-2 (6000 IU/mL)	+
	OKT-3 (30ug) added on Day 7	+
	Feeders Added on Day 7	500 E06
	Total Feeders at Day	750 E+06
Process Day	Conditions	Gen 3.1 Test
Day 9-11 - Scale Up	From G-REX 100MCS transfer TIL suspension to 1 G-REX 500MCS (up to 3 GREX 500MCS)	Yes
Day 16 - Harvest	LOVO- automated cell washer	Yes

Figure 20

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*Figure 21*

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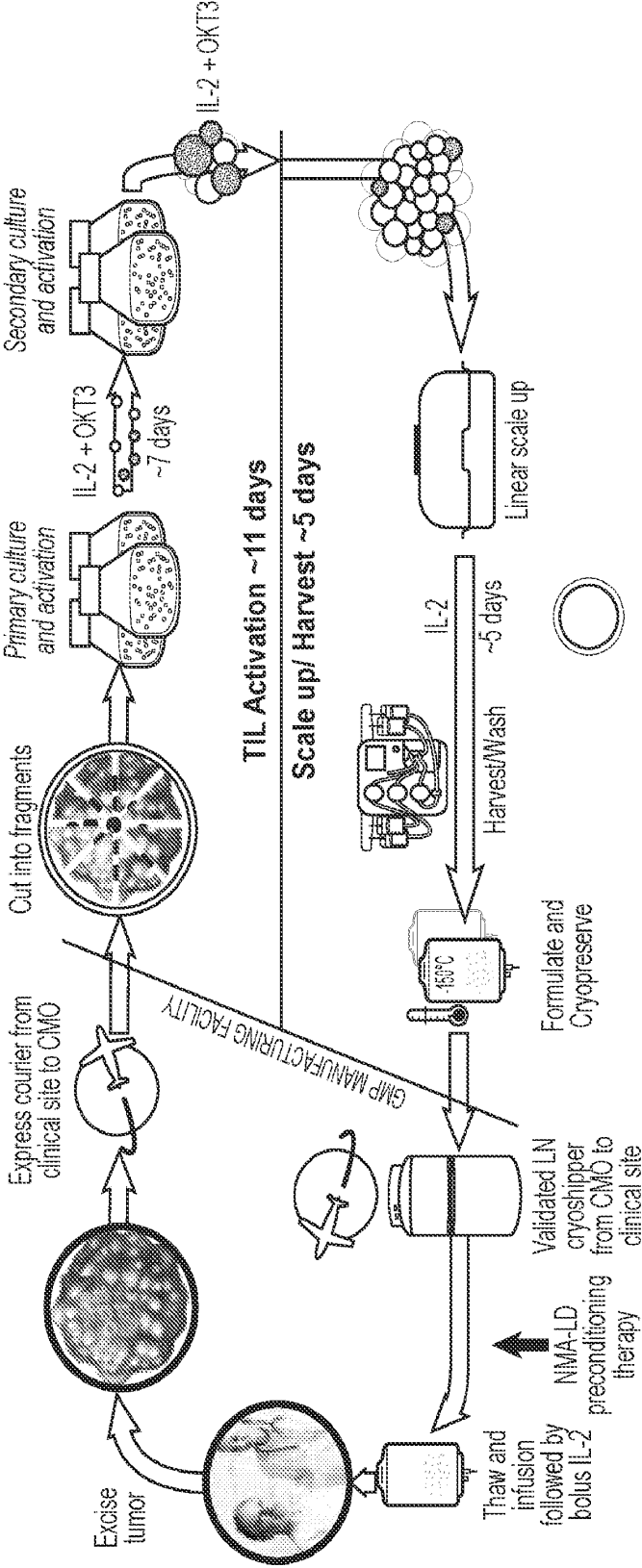


Figure 22

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	Gen 2	Gen 3
Total culture time	22 days	16-17 days (or 16 days)
Pre-REP		
Fragments/flask	≤ 60 fragments in one flask	≤ 60 fragments in up to 4 flasks
Media volume	1L – single addition	1L – 2 x 500 mL additions
Target pre-REP cell numbers	<200 x 10 ⁶ TIL	All cells carried through continuous process
Screening	No screen	No screen
Selection of flasks	No selection	Bact-T sterility, visual inspection for contaminants
REP/Scale up		
Feeders		Reduced by ≥ 40%
Media	Contains HSAB	Defined medium
Scale up	Pooled culture; volume reduce to 500 mL on Day 5 split up to 5 flasks (2500 cm ²)	Flasks scaled linearly and treated as subcomponents
OKT3	150 µg	≤ 180 µg
IL-2	High dose	High dose
Number of flasks	1-5	1-4
Final steps		
Harvest/volume reduction	Closed 10:1	Closed 10:1
Concentrate/wash	LOVO 100:1	LOVO 100:1
Formulation conditions	1:1 CS10 (5% DMSO)	1:1 CS10 (5% DMSO)
Shipment conditions	Vapor phase liquid nitrogen	Vapor phase liquid nitrogen
Infusion	Thawed IV gravity	Thawed IV gravity

Figure 23

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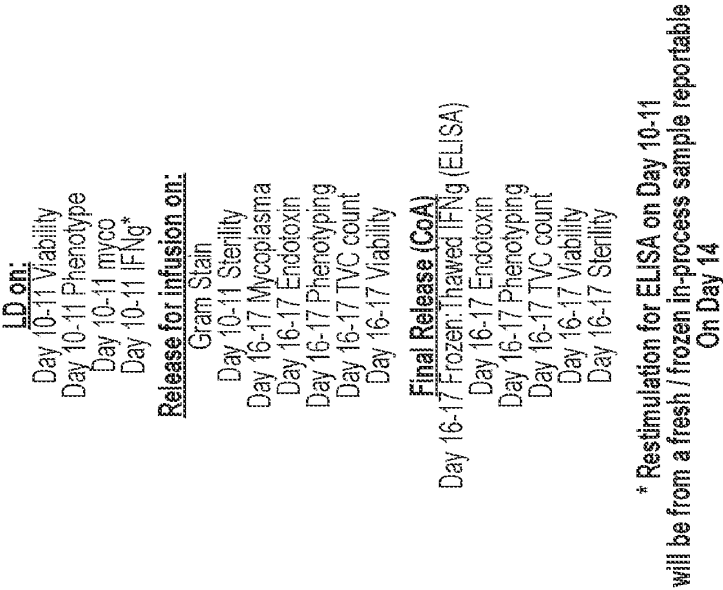


Figure 24

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Day 0: Pre-
REP

Fresh/Frozen Tumor
1-4 flask GREX-100MCS up to
60 fragments per flask
500mL of CM1+6,000 IU/mL IL-2
+OKT3 (15 ug)
+250 E6 feeder cells

Day 7: Pre-
initiation

Direct to REP – each GREX
100MCS
Add 500 mL CM2+6,000 IU/mL IL-2
Feeder cells 5E8 cells/flask
30ng/mL OKT3 (30ul)

Day 10 to 11:
TIL-Scale Up

Scale up each GREX 100MCS to
GREX 500MCS, Transfer all cell
suspension to GREX500MCS and
add 4L of CM4 + 3,000 IU/mL of IL-2

Day 14-16:
Harvest

Harvest-LOVO
automated cell
washer

Figure 21

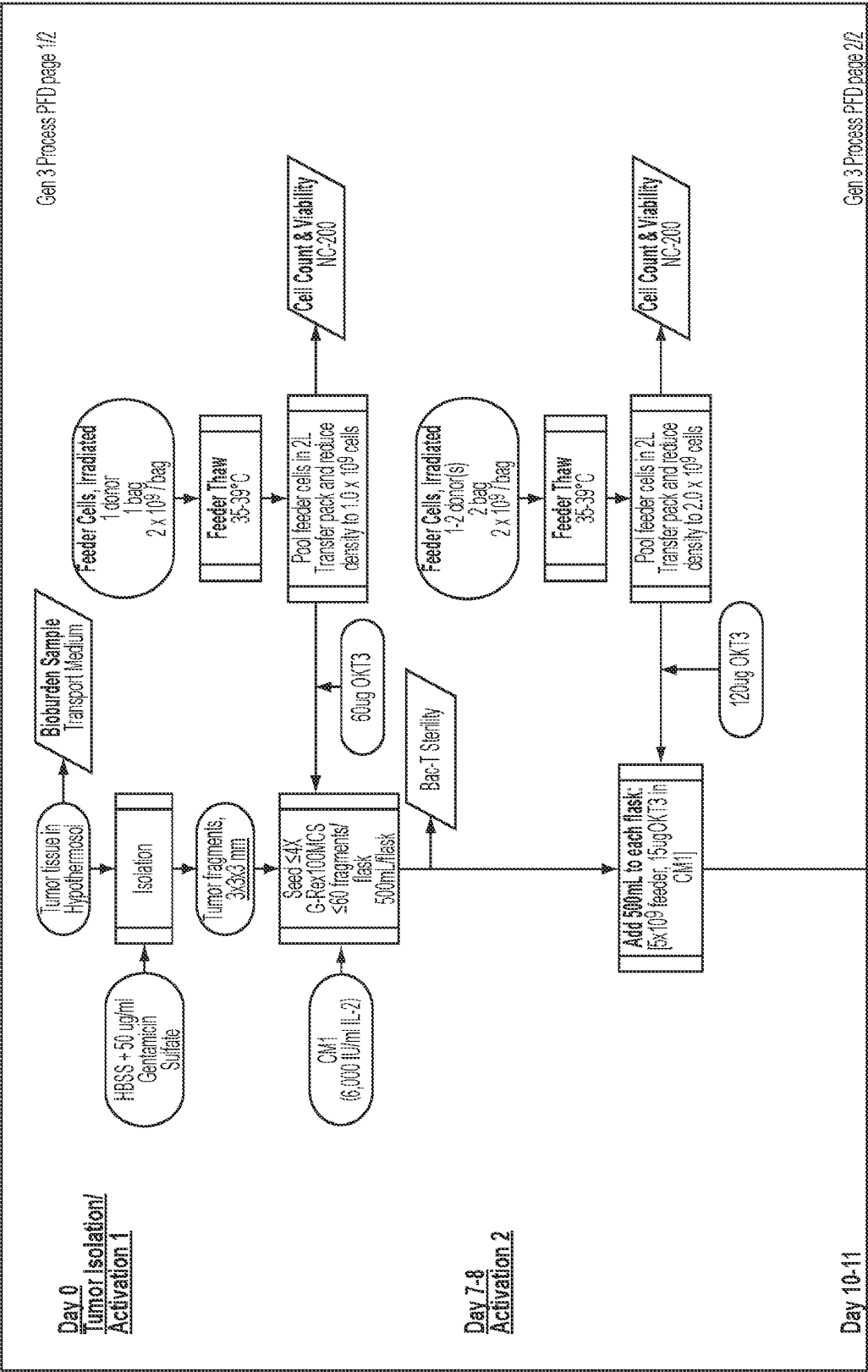


Figure 26A

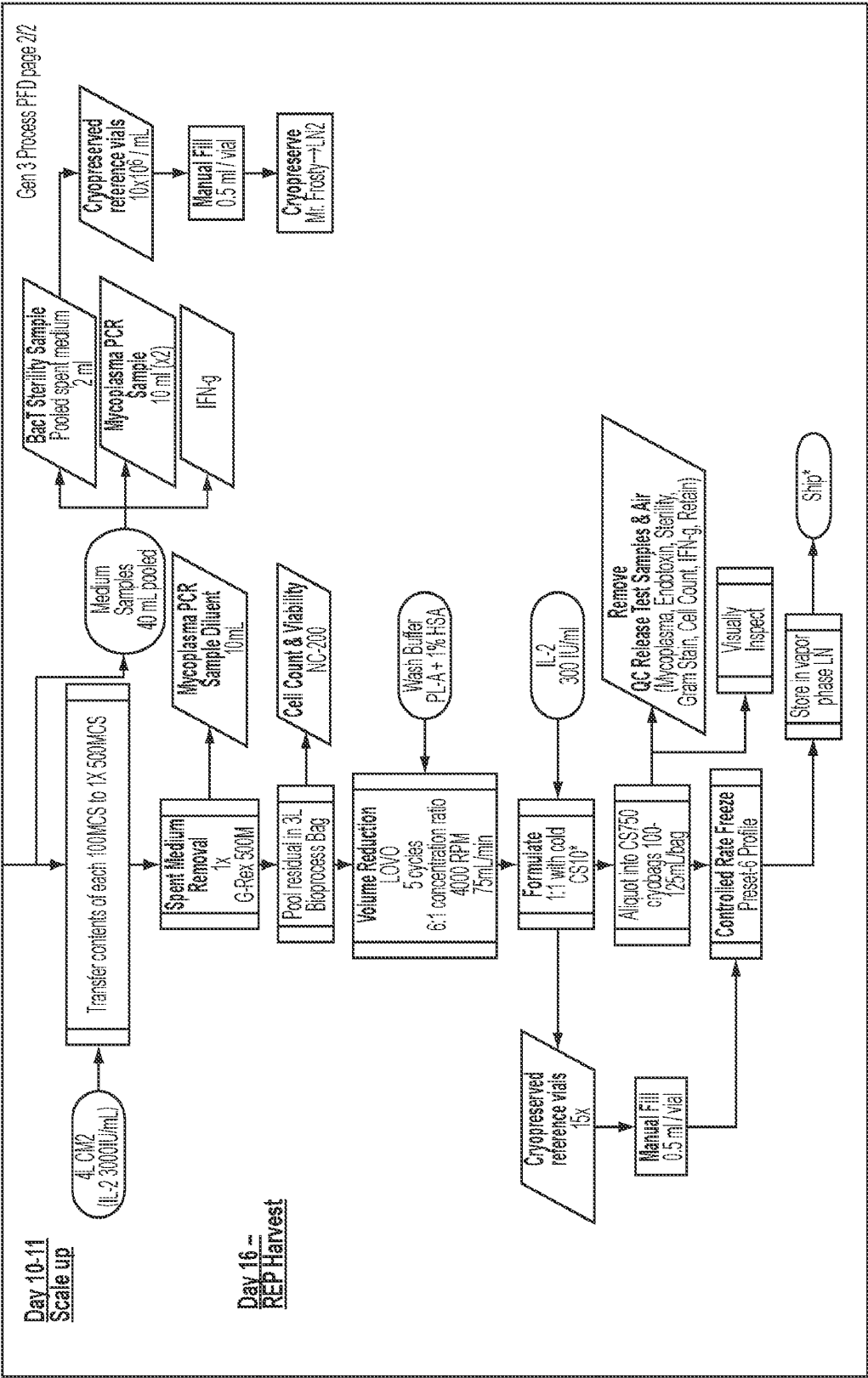


Figure 26B

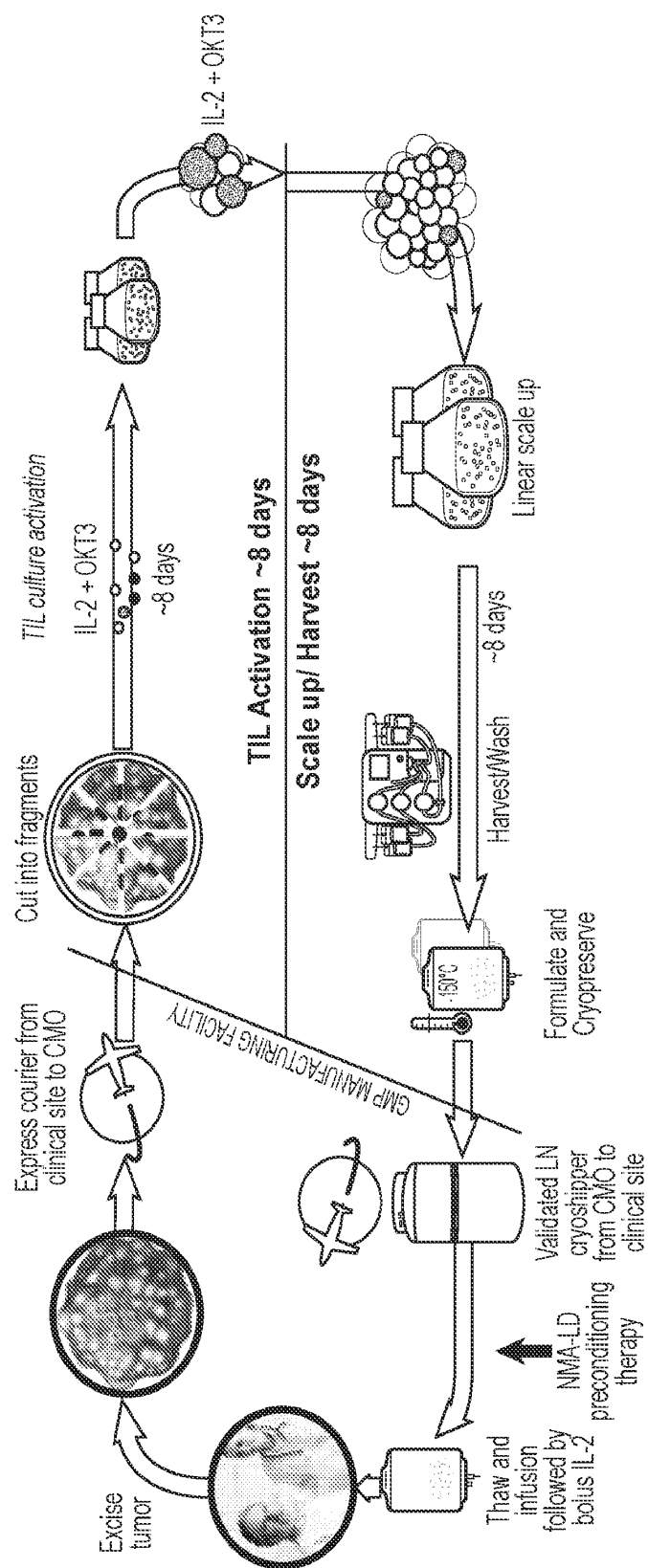


Figure 27

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STEP	Gen 2	Gen 2.1	Gen 3.0
Pre REP- day 0	≤ 50 fragments/ 1 G-Rex 100MCS - 11 days	≤ 180 fragments/ 3 G-Rex, Pre-formulated CM1 warmed media 100MCS - 11 days	Fresh or Frozen Tumor Whole tumor with ≤ 30 fragments up to 60 fragments per 1 G-Rex. 100MCS (up to 4 G-Rex), preformulated warmed media - 7 days. Pre REP, Feeders 250e6 cells + OKT-3 (15ug)
REP Initiation	Direct to REP - Day 11- <200e6 TIL 1 G-Rex 500MCS	Direct to REP - Day 11- <200e6 TIL Pre-formulated CM2 warmed media in one G-Rex 500MCS	Direct to REP - Day 7-all cells TIL- same G-Rex 100MCS (100MCS up to 4 GREX), Standard media or Defined Media (Serum free). Addition Feeders 500e6 cells +OKT-3 (30ug)
TIL propagation or Scale up	1 to 5 G-REX 500MCS Split day 16	2 to 5 G-REX 500MCS Pre-formulated CM4 warmed media Split day 16	From G-REX 100MCS transfer TIL suspension to G- REX 500MCS, up to 4 GREX 500 MCS- Standard media or Defined Media (Serum Free) Scale up on day 10 or 11
Harvest	Harvest day 22, LOVO-automated cell washer	Harvest day 22, LOVO-automated cell washer (5 wash cycle)	Harvest day 14 or 16 LOVO- automated cell washer (5 wash cycle)
Final formulation	Cryopreserved Product 300IU/ml IL2- CS10 in LN ₂ , multiple aliquots	Cryopreserved Product 300IU/ml IL2- CS10 in LN ₂ , multiple aliquots	Cryopreserved product 300IU/ml IL-2- CS10 in LN ₂ , multiple aliquots
Process time	22 days	22 days	16 days

Figure 28

Process Comparison	Process Changes	Differences
Gen 2 : Gen 2.1	• Initiate process with two flasks instead of one flask • Divide REP initiation feeder layer between 2 G-Rex500MCS Flasks • Pre-formulate media and warm prior to use	• Potential doubling of final cell count (dose with increased TIL repertoire. • Process redundancy throughout process
Gen 2.1 : Gen 3.1	• Fresh or Frozen tumor • 14-16 day process (from 22 day) • Reduce total feeder layer on process • Feeder layer and OKT3 present at Day 0 • REP initiated with fragments • 100MCS scales to 500MCS • Scales to multiple pre-REP flasks • Standard Media and Defined Media (Serum Free)	• Increased potency • Improved phenotype • Decreased process time • Reduced reagent testing • Decreased process variability • Defined reagents • Increased repertoire • Reduce impurities (feeder) • Comparable or Higher Dose.

Figure 29

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TABLE 4. DESCRIPTION OF CELL CULTURE CONDITIONS.

Process Day	Conditions	Gen 3.0	Gen 3.1 control	Gen 3.1 Test
Day 0 : Tumor Fragment Isolation and Activation	Media (*)	500 mL	500 mL	500 mL
	IL-2	6000 IU/mL	6000 IU/mL	6000 IU/mL
	OKT-3	-	15 ug	15 ug
	Feeders	-	-	2.5E+06
Process Day	Conditions	Gen 3.0	Gen 3.1 control	Gen 3.1 Test
Day 7 - 8 : TIL Culture Reactivation	Media (*)	500 mL	500 mL	500 mL
	IL-2	6000 IU/mL	6000 IU/mL	6000 IU/mL
	OKT-3	30 ug	30 ug	30 ug
	Feeders	1 E+09	500 E+06	500E+06
	Total Feeders added through Day 7	1 E+09	500 E+06	750E+06
Process Day	Conditions	Gen 3.0	Gen 3.1 control	Gen 3.1 Test
Day 10-11 : Culture Scale Up	From GREX 100 transfer whole TIL suspension to 1 GREX 500 containing 4L media with IL-2 (3000 IU/mL)			
Process Day	Conditions	Gen 3.0	Gen 3.1 control	Gen 3.1 Test
Day 16-17: Harvest/Wash/Formulate	LOVO automated cell washer and cryopreservation with CS10.			

(*) Media can be standard media or CTS serum free media.

Figure 30

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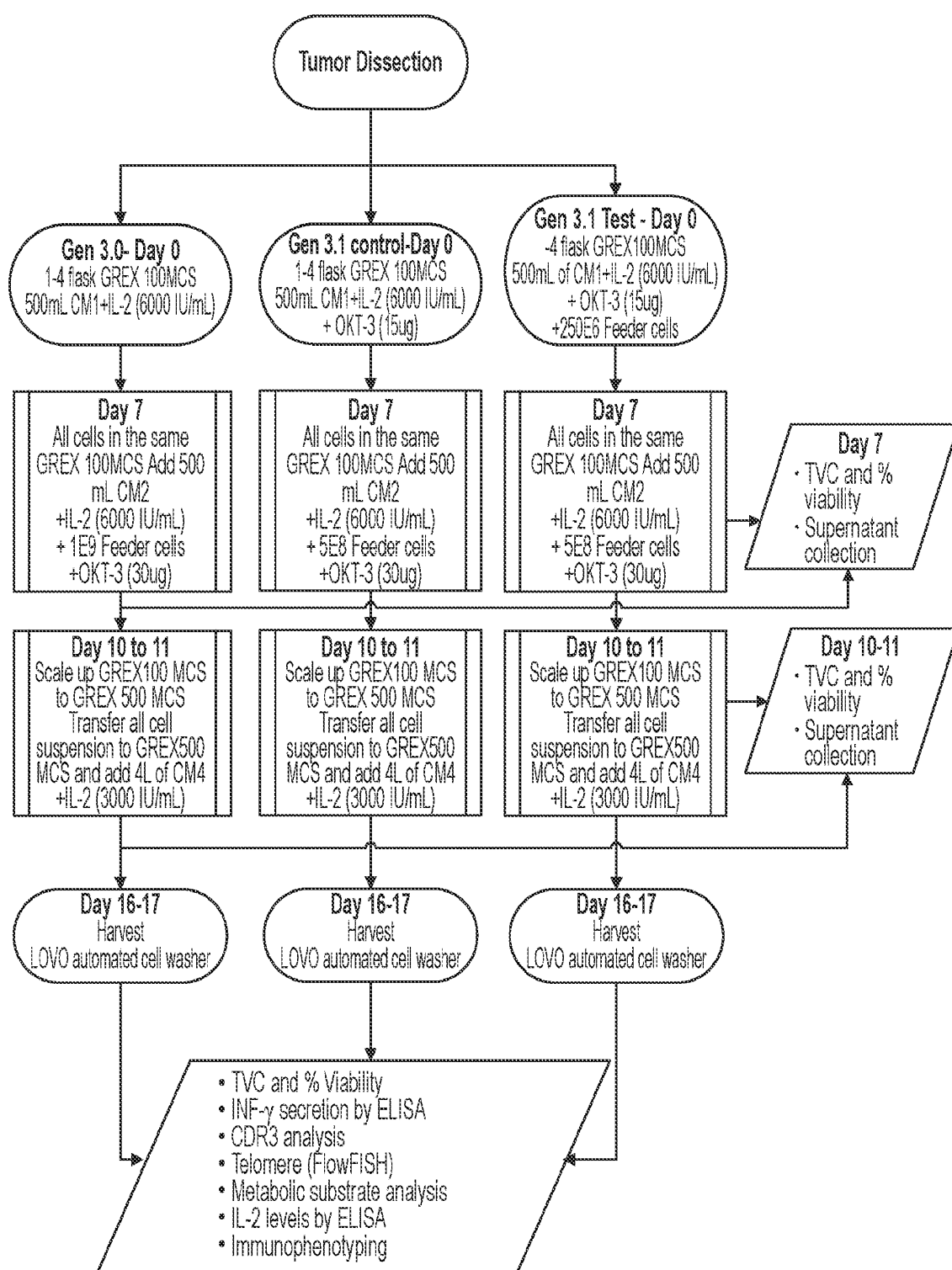


Figure 31

Step	Process Gen 3-Optimized
Day 0 Tumor isolation and Activation	≤240 fragments ≤60 fragments/flask ≤4 flasks ≤2L media (500mL/flask) IL-2 (6000IU/mL) 2.5x10 ⁸ feeder cells/flask 15ug OKT3/flask
Day 7 - 8 Reactivation	Fresh TIL direct to REP Activate entire culture 5x10 ⁸ feeder cells 30 ug OKT3/flask G-Rex 100MCS Add 500mL media+ IL-2(6000IU/mL)
Day 10 - 11 Scale up or TIL Sub-culture	≤4 G-REX 500MCS Scale up entire culture transferring 1L from GREX 100MCS into GREX 500MCS and add 4L of media +IL-2 (3000 IU/mL) /flask
Day 16 - 17 Harvest	Harvest LOVO- automated cell washer Cryopreservation on Plasmalyte 1% HSA: CS10

Figure 32

Test	Acceptance Criteria	Gen 3.1 Test vs Gen 3.0 Process
Cell Count (TVC)	Gen 3.1 > 30% to Process Gen 3.0	Met
% Viability	≥70% Viability	Met
Immunophenotyping (%CD3+/- %CD45+)	≤5% difference between Gen 3.1 and Gen 3.0 process	Met
IFNγ secretion	Gen 3.1 ≥ to Process Gen 3.0	Met

Figure 33

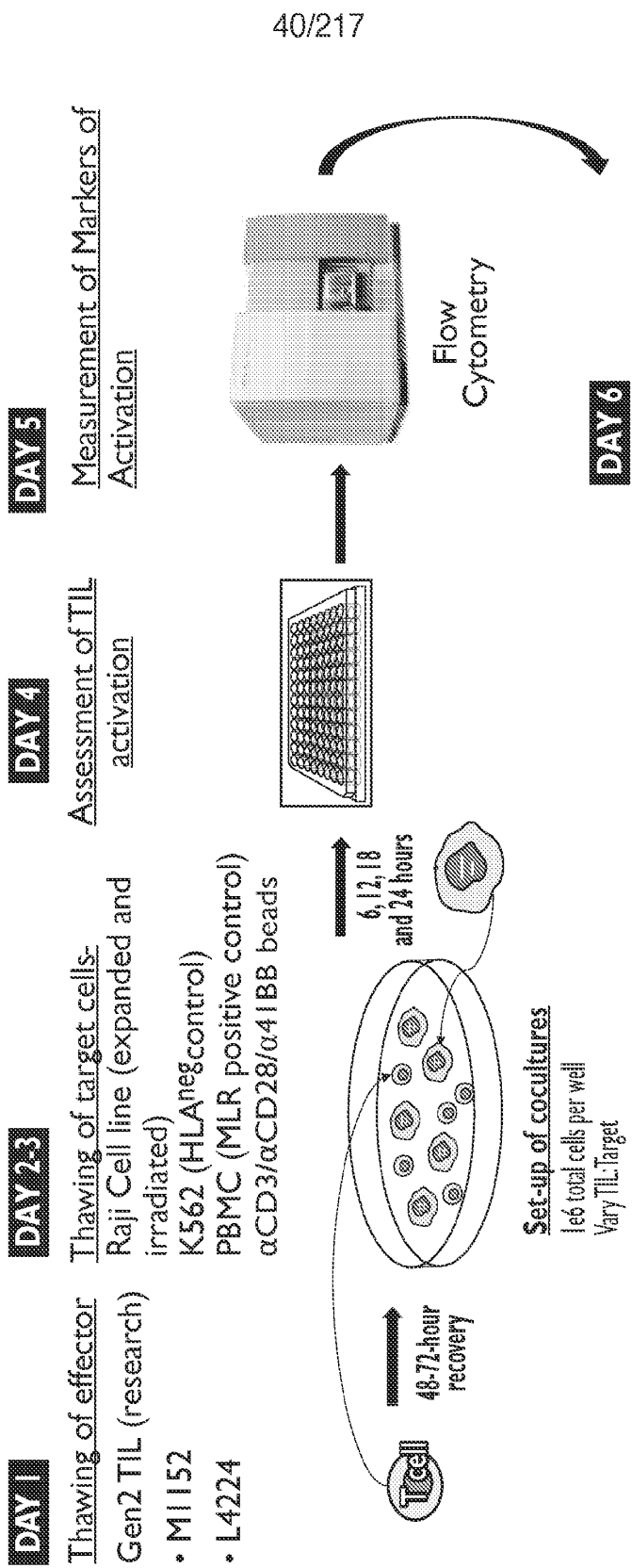


Figure 34

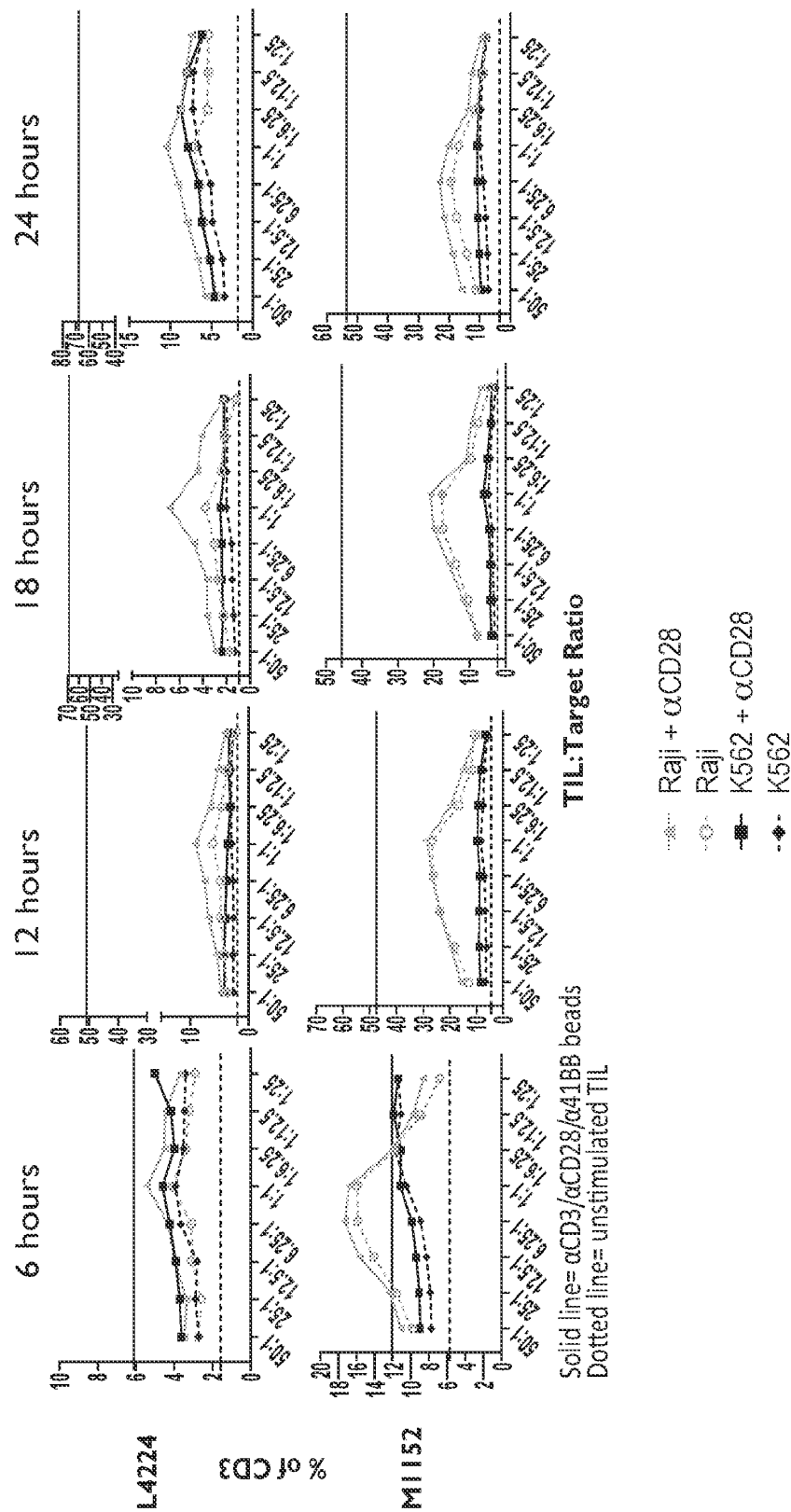


Figure 35

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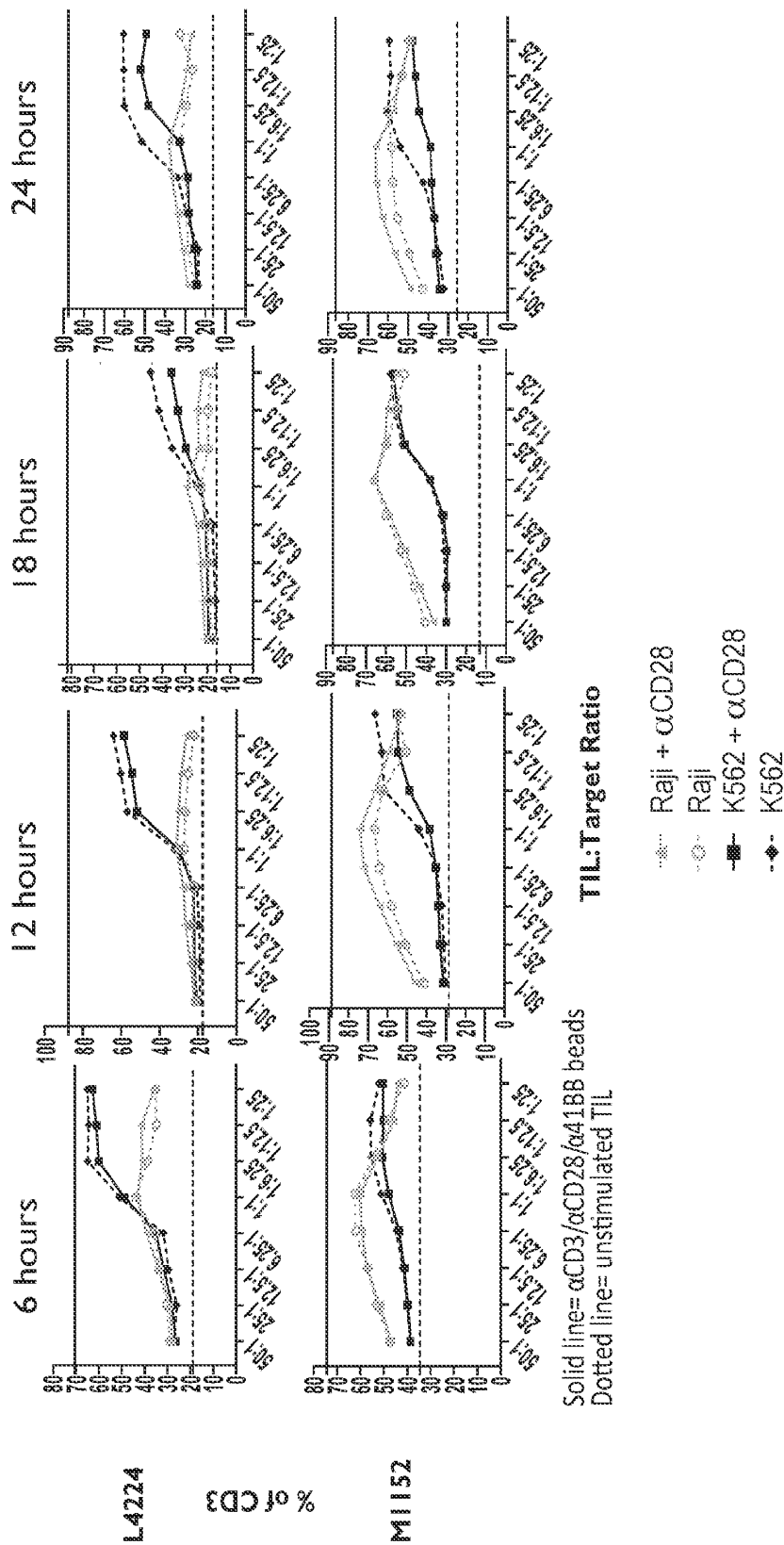


Figure 36

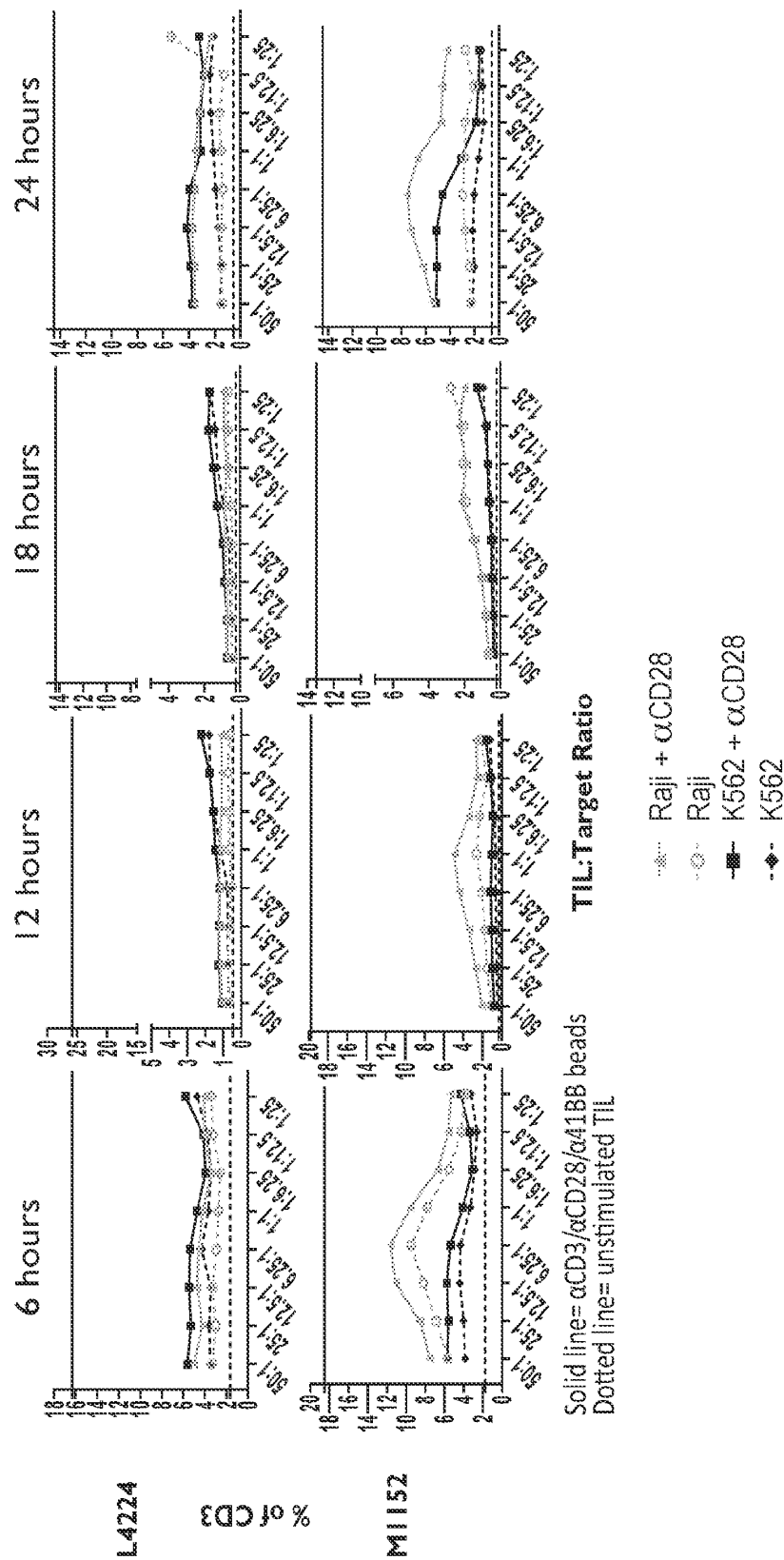


Figure 37

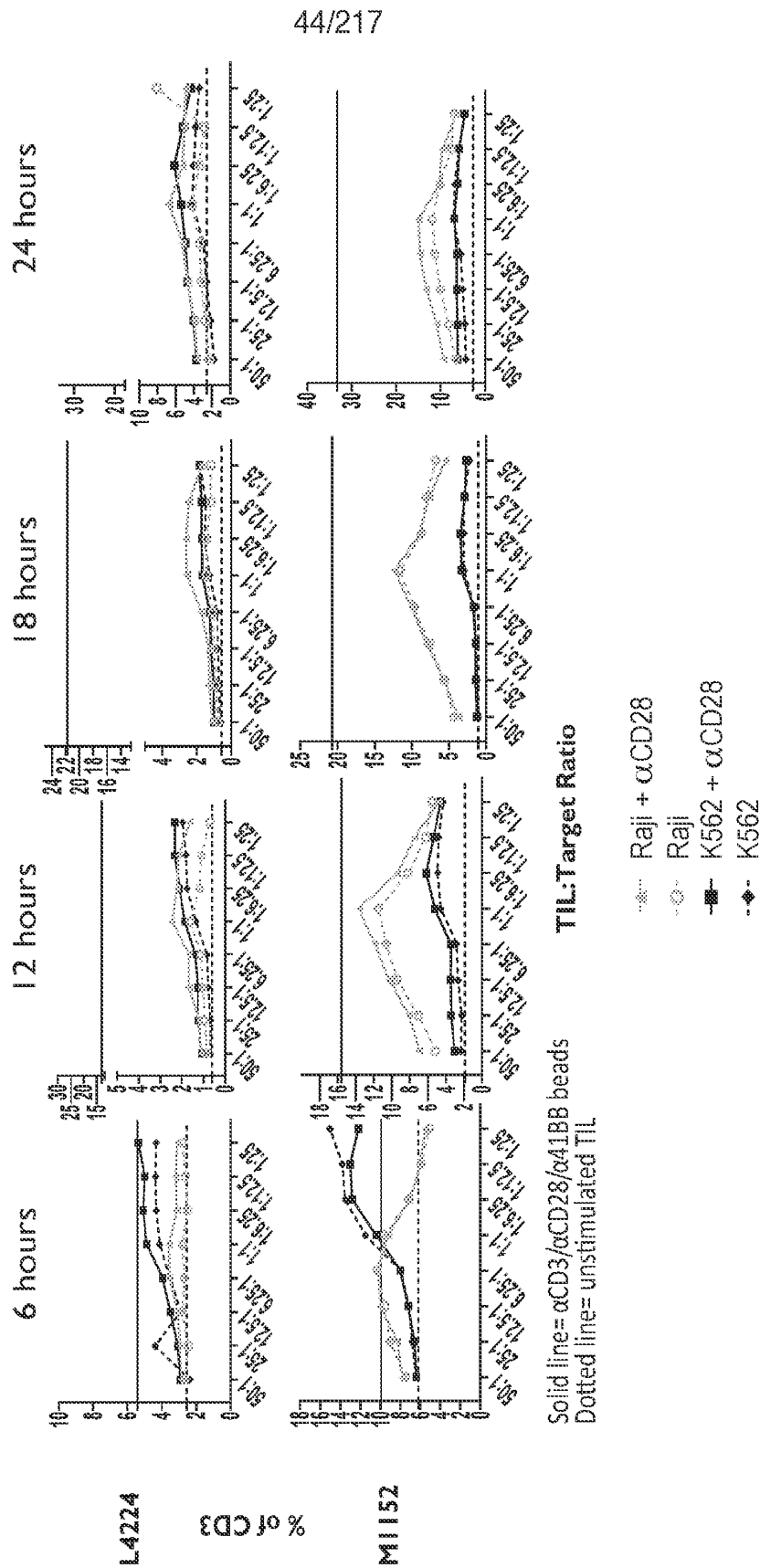


Figure 38

45/217

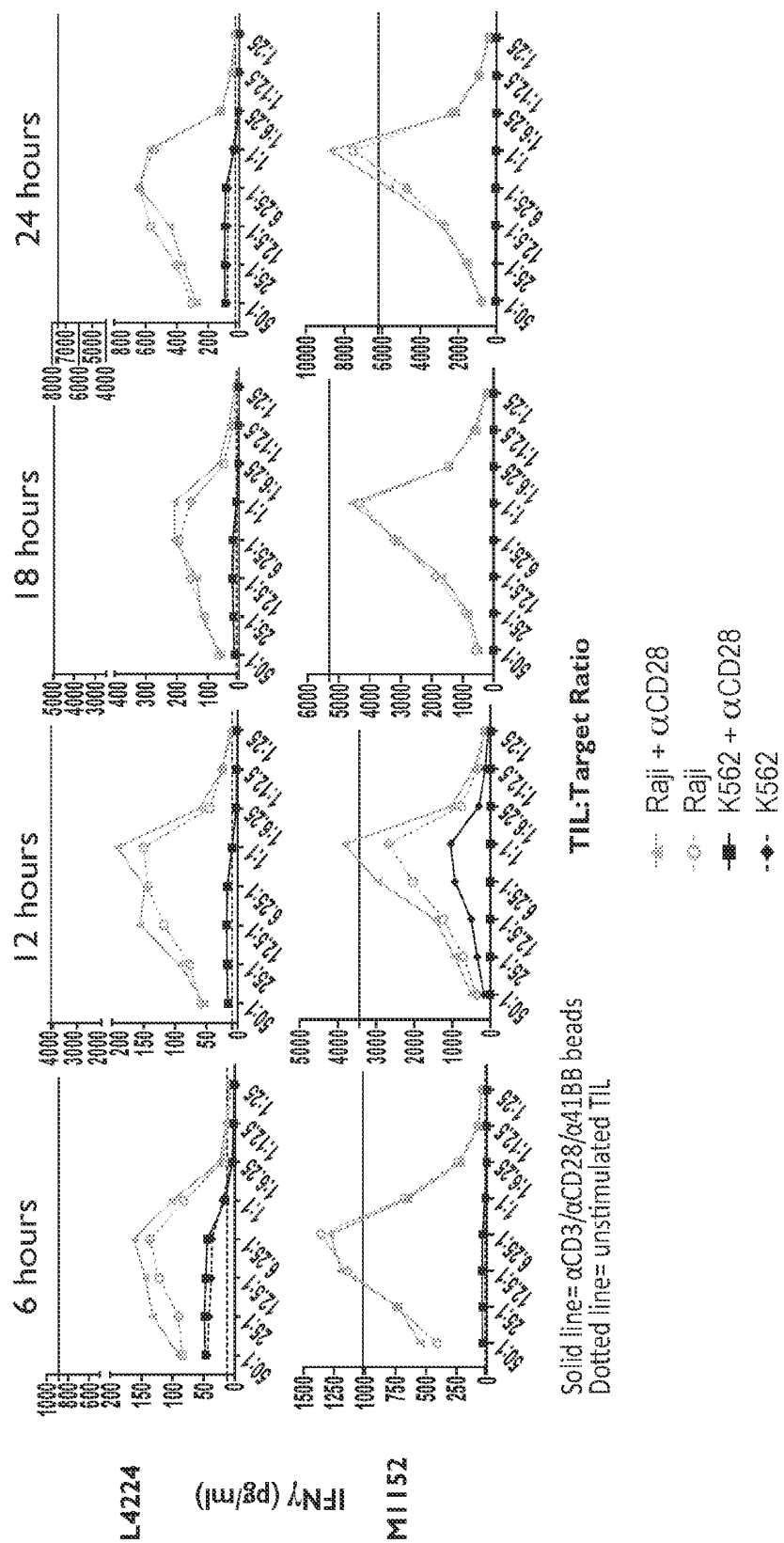


Figure 39

46/217

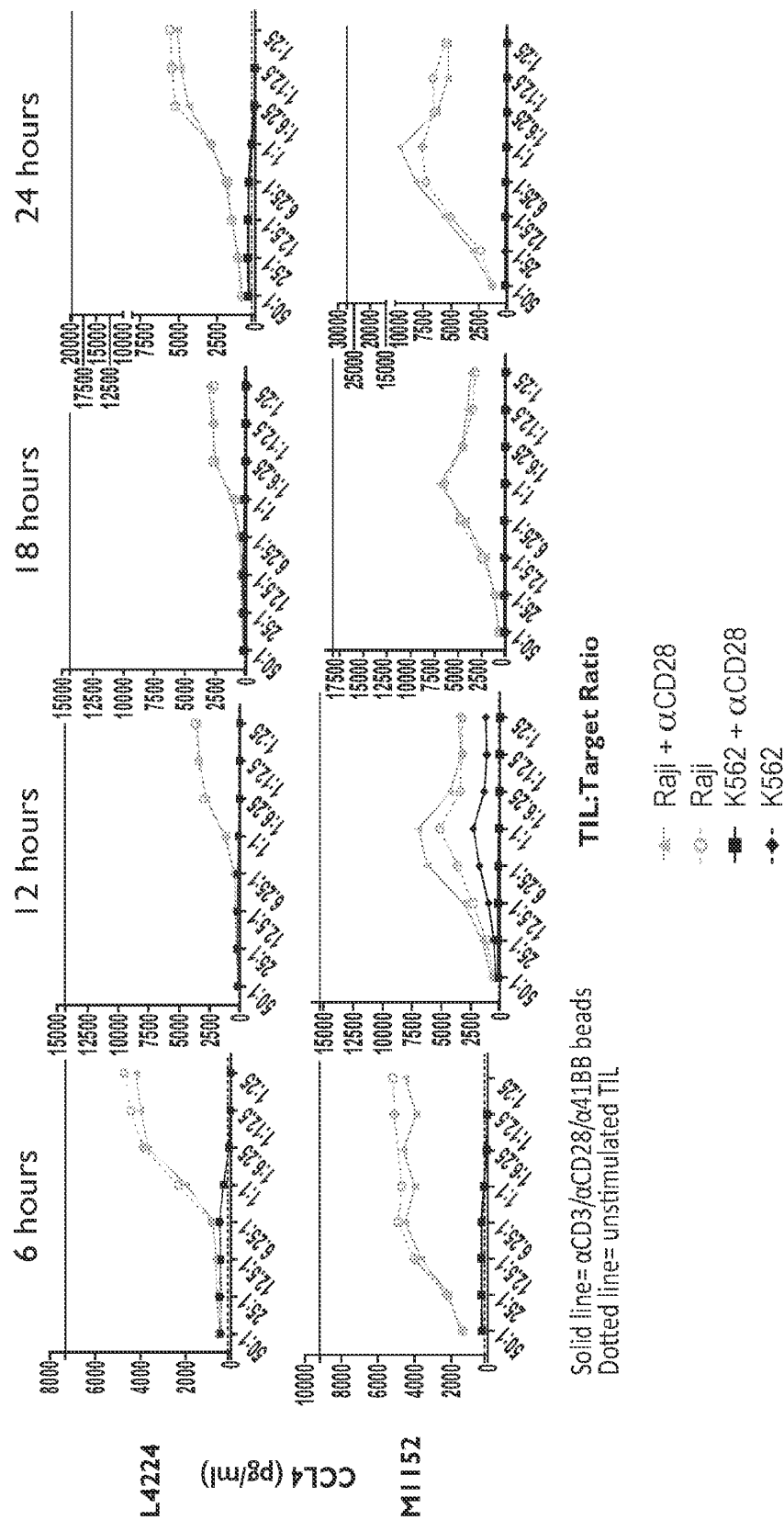


Figure 40

47/217

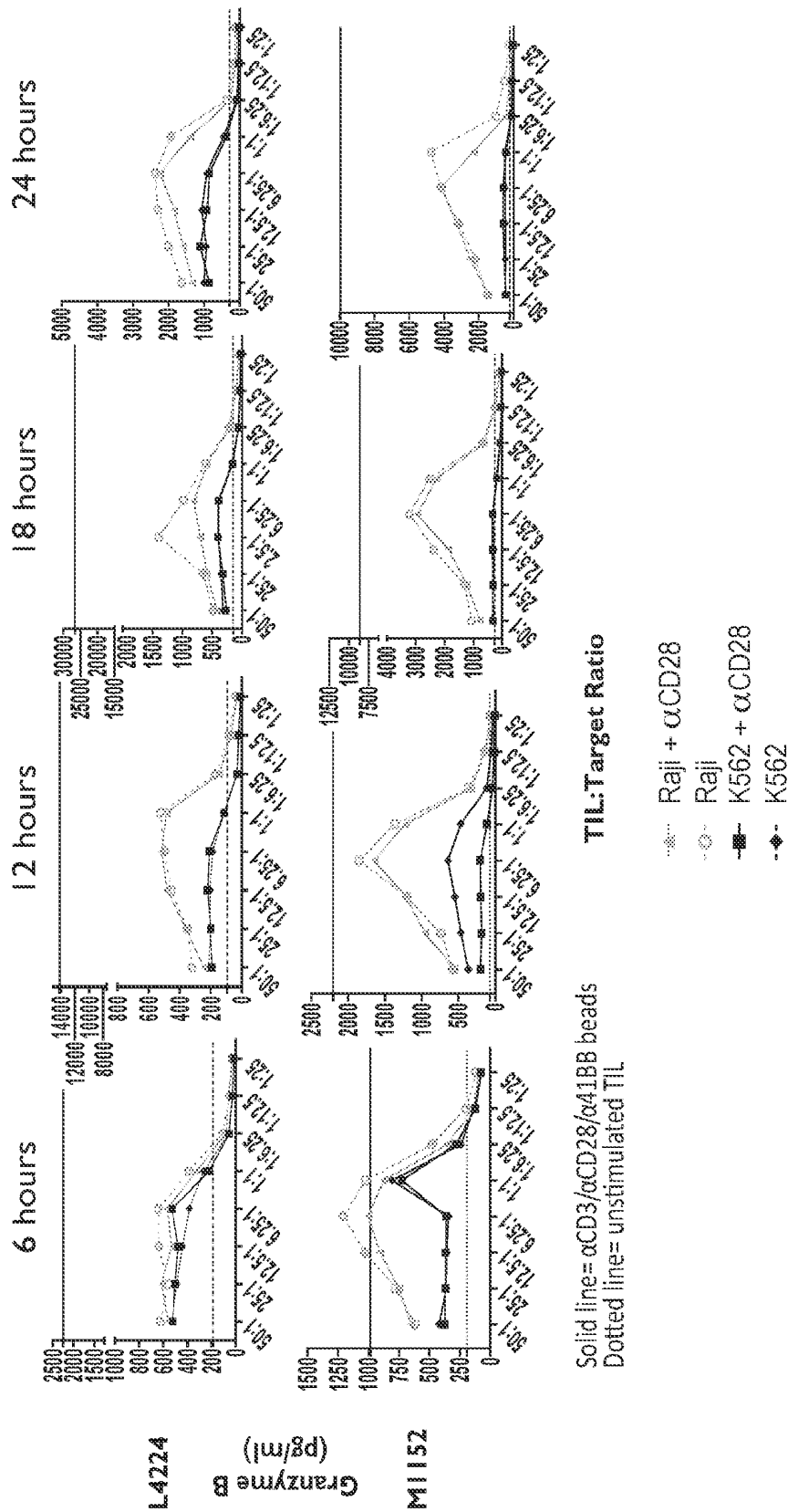


Figure 41

48/217

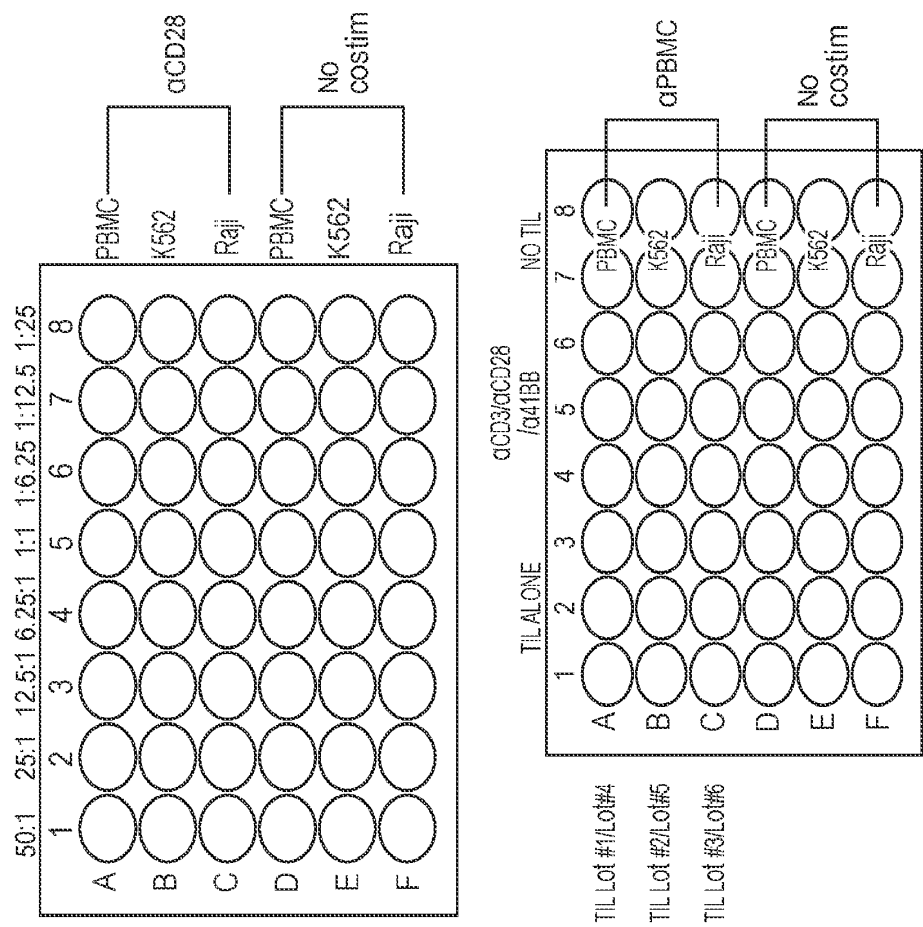


Figure 42

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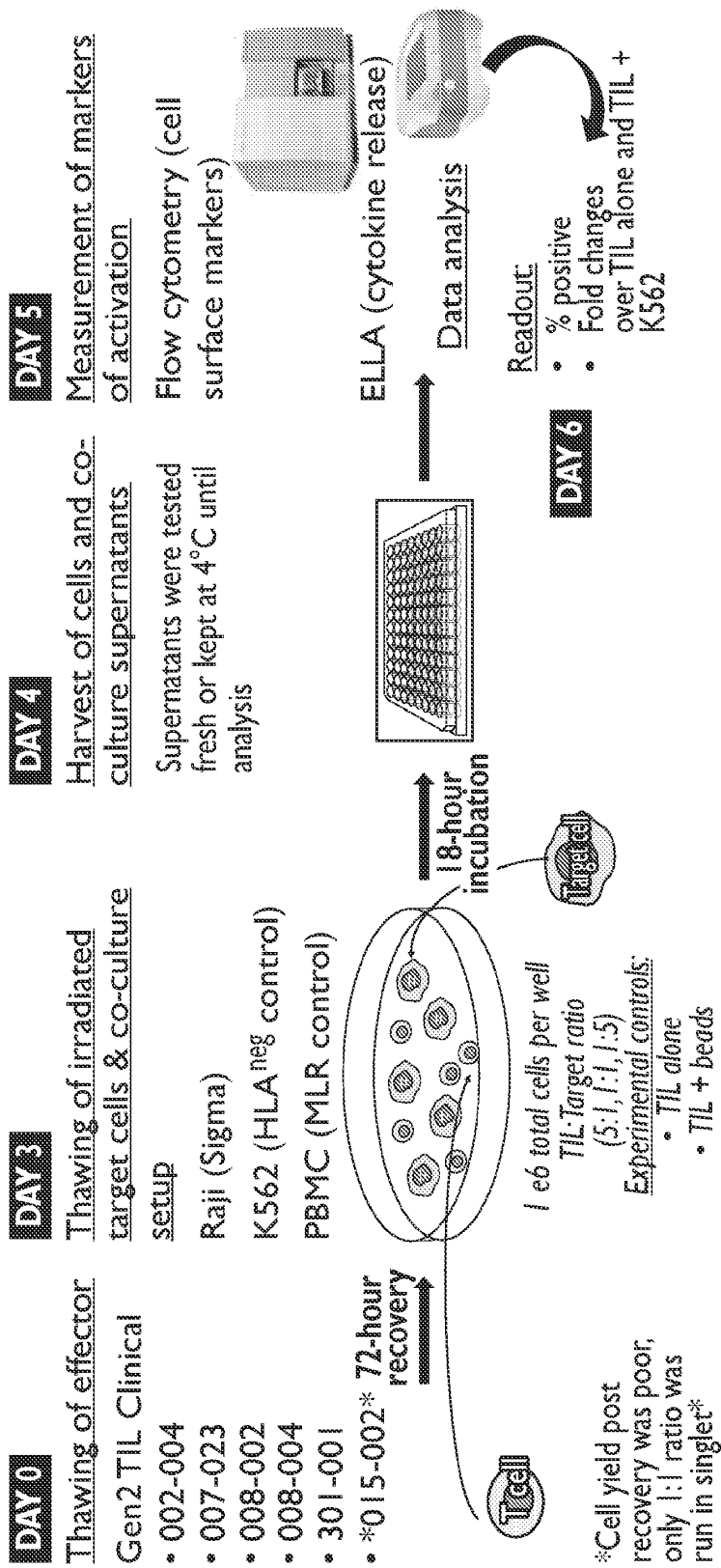


Figure 43

50/217

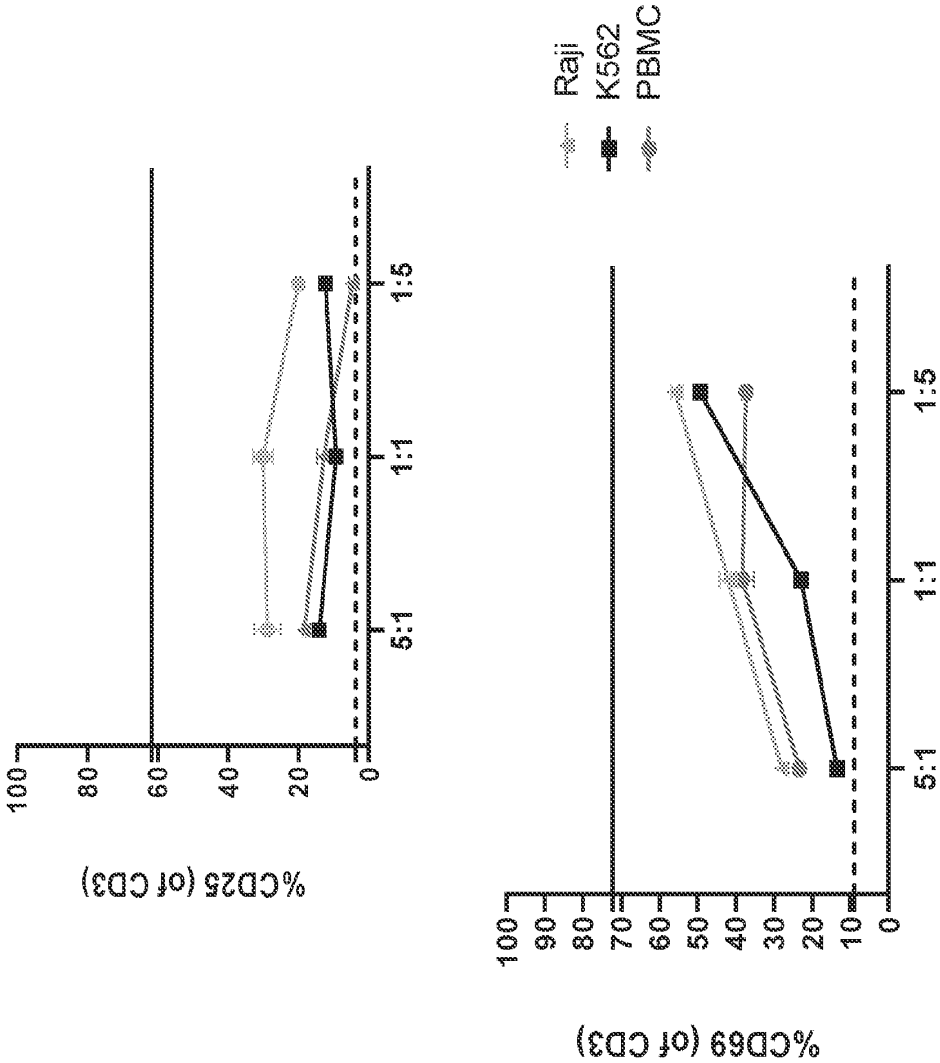


Figure 44

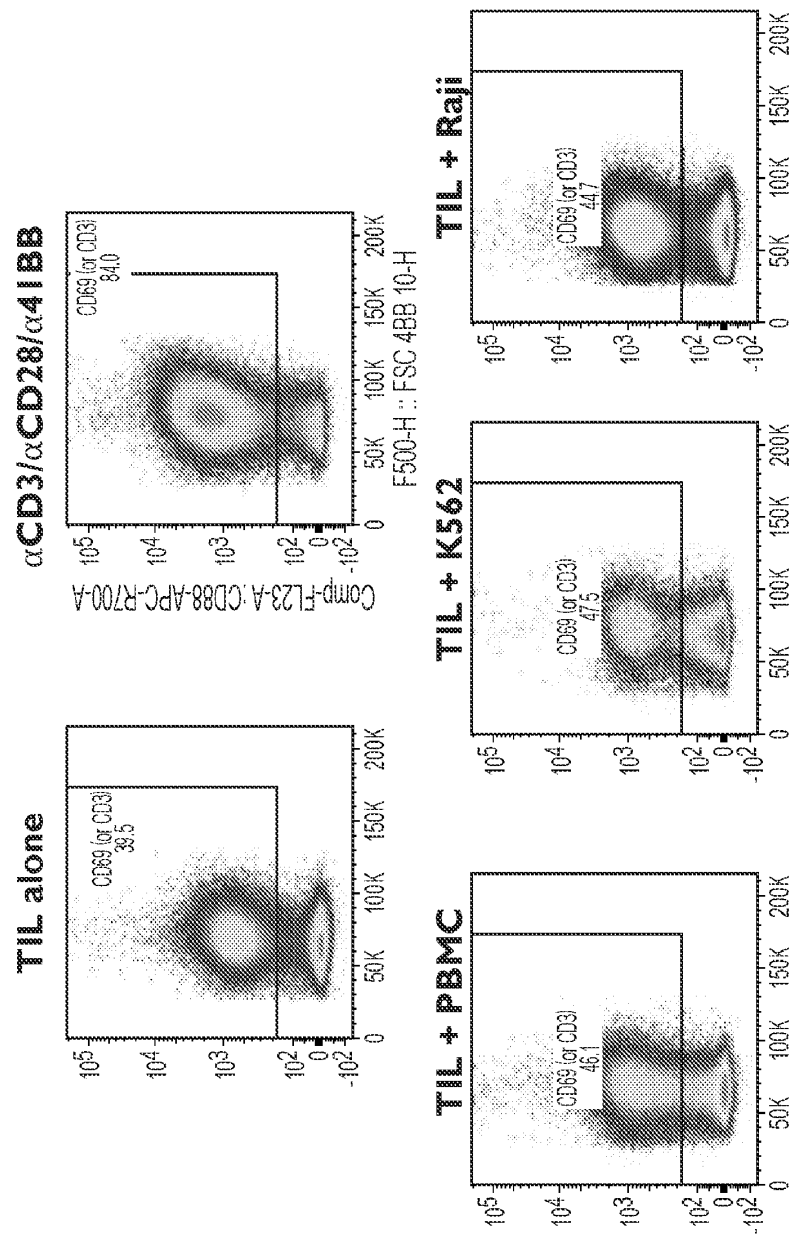


Figure 45

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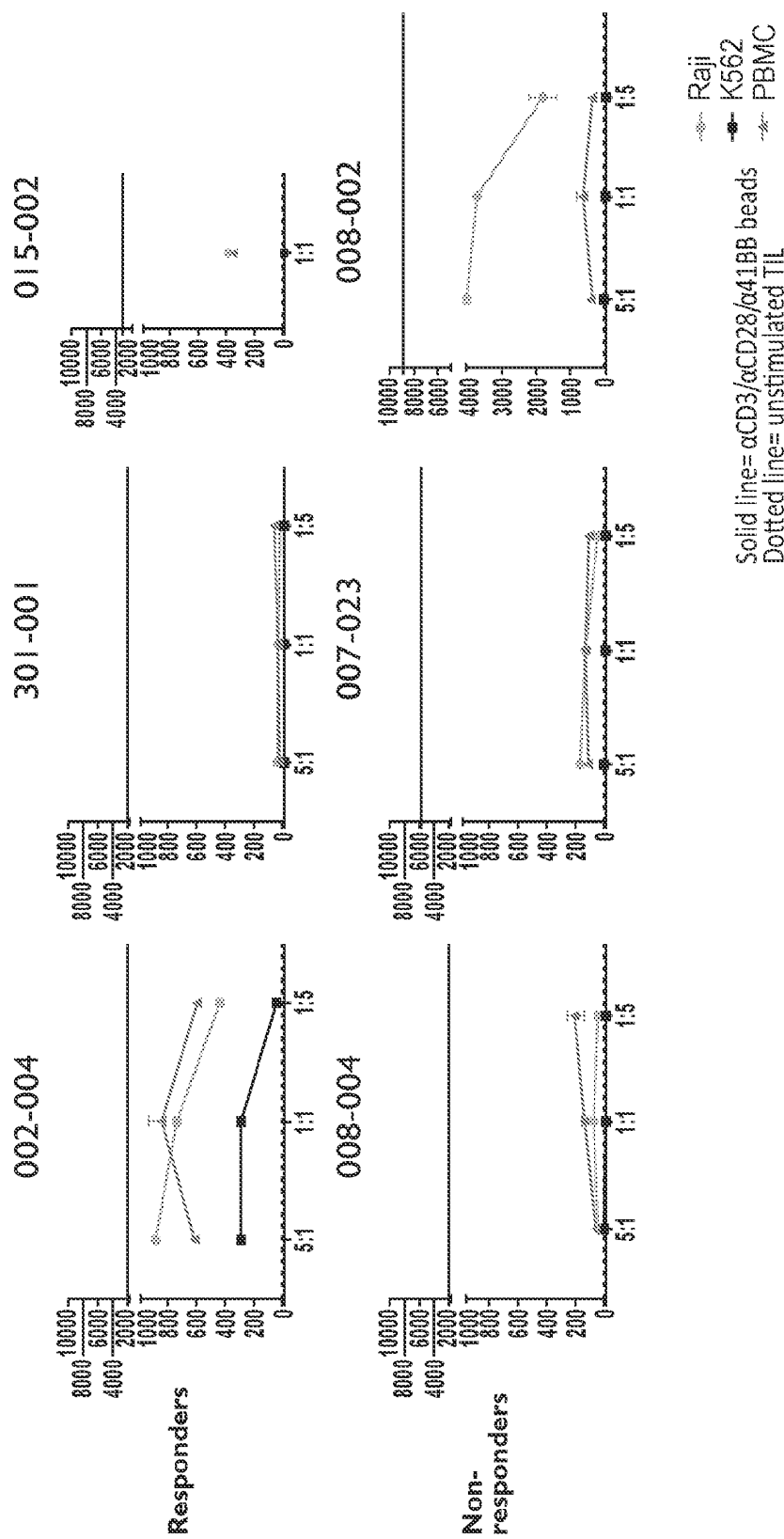


Figure 46

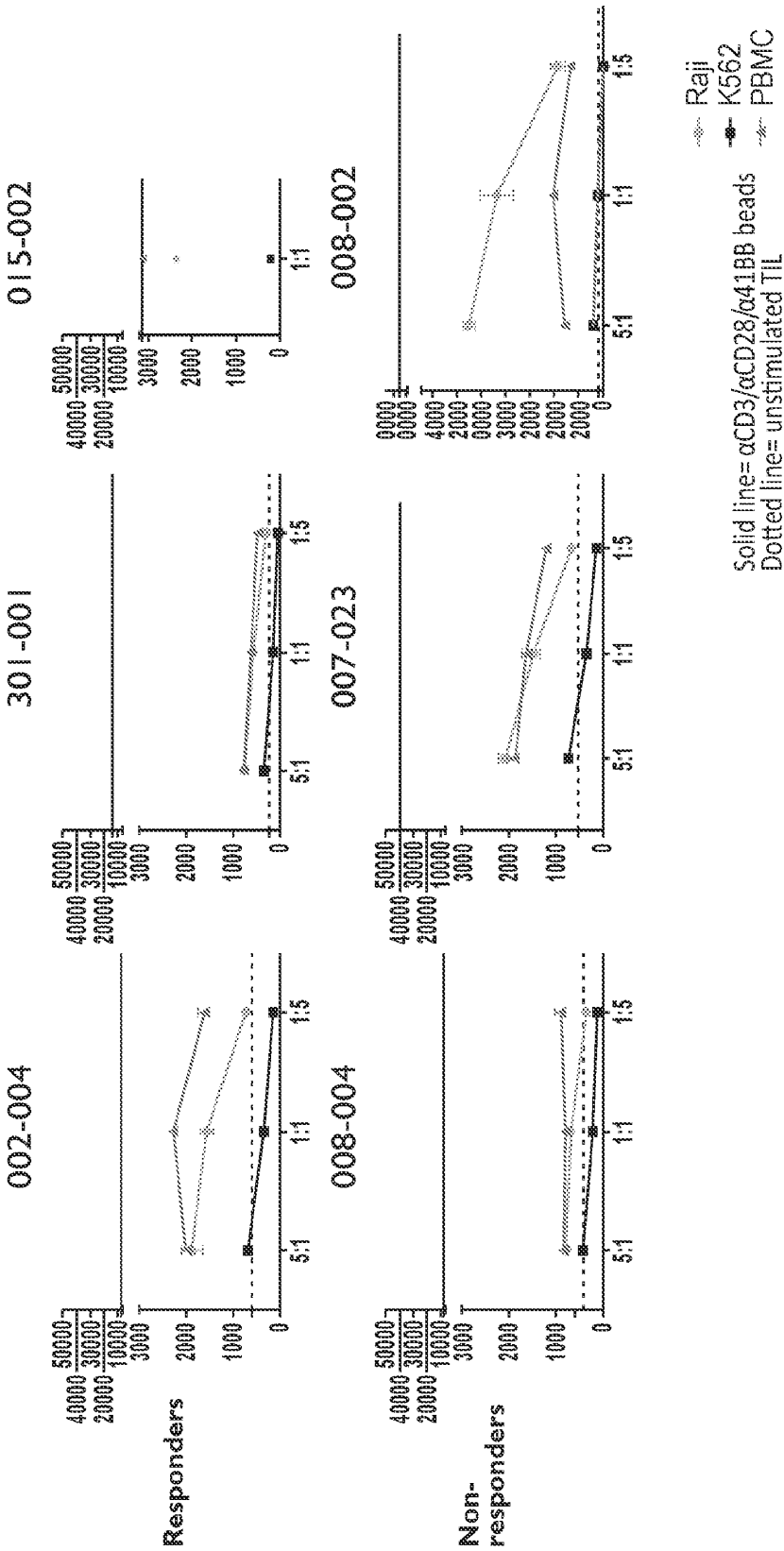


Figure 47

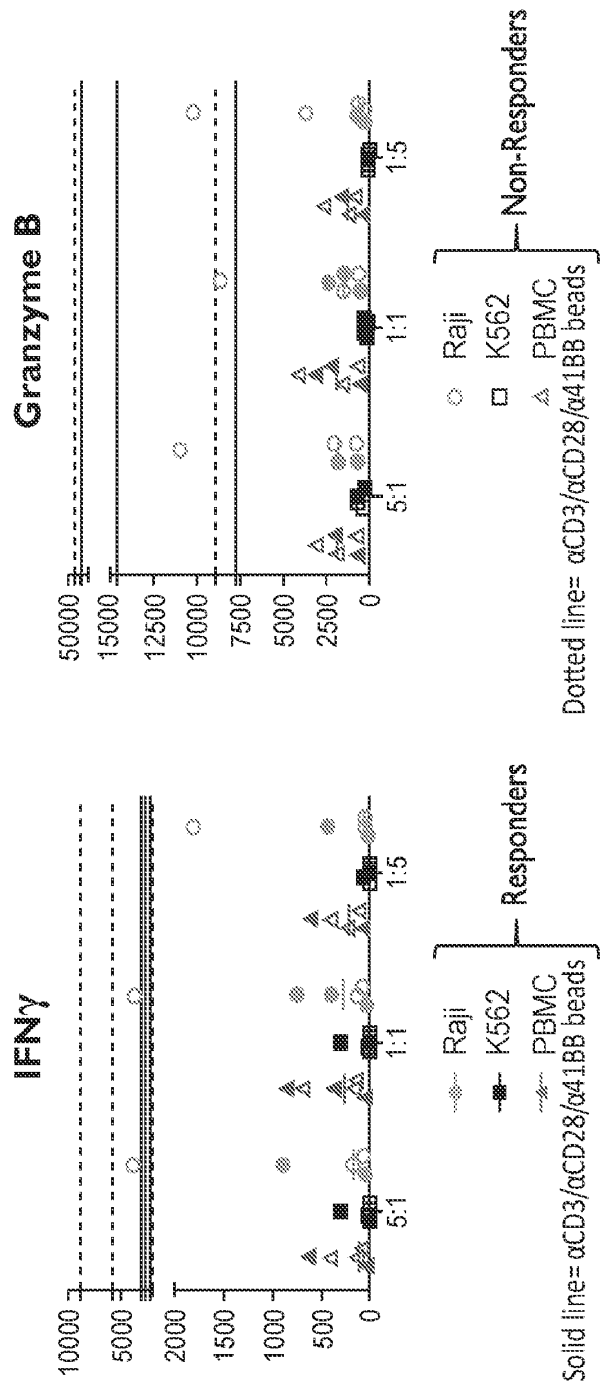


Figure 48

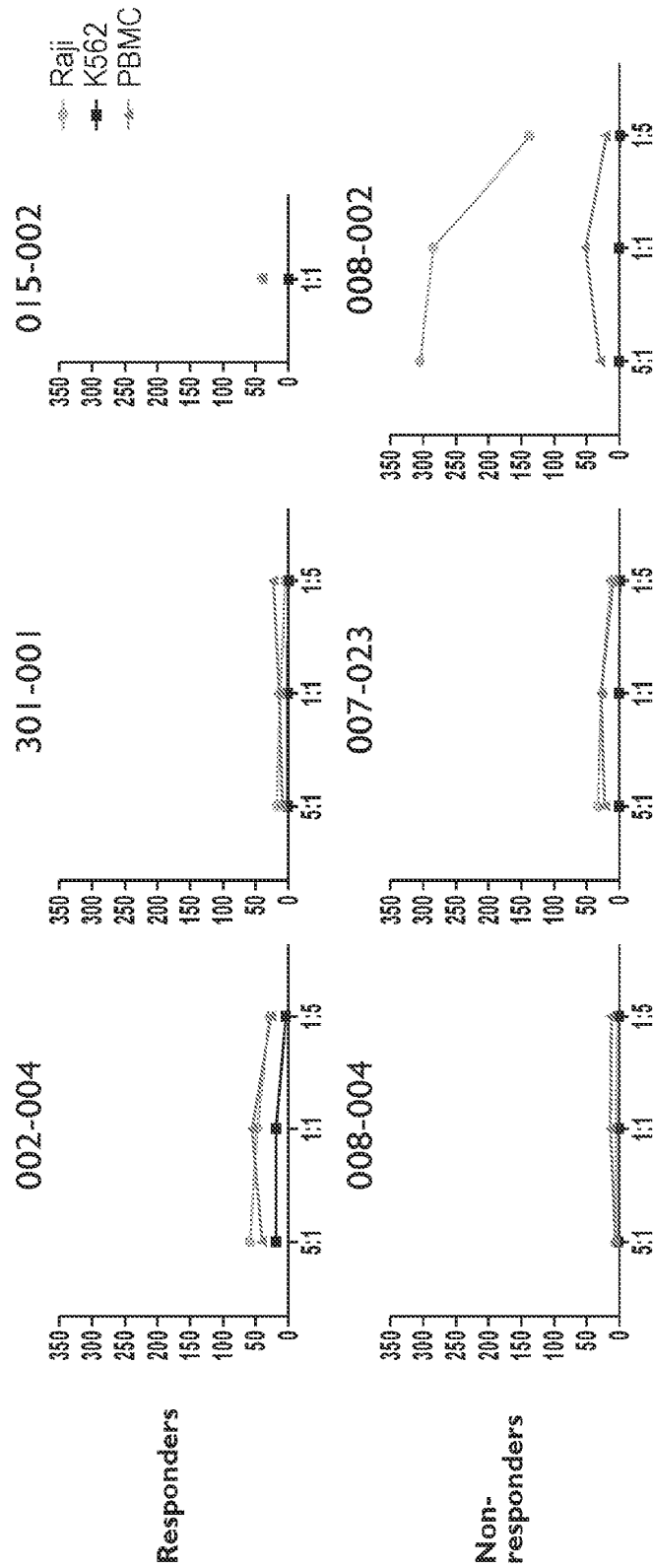


Figure 49

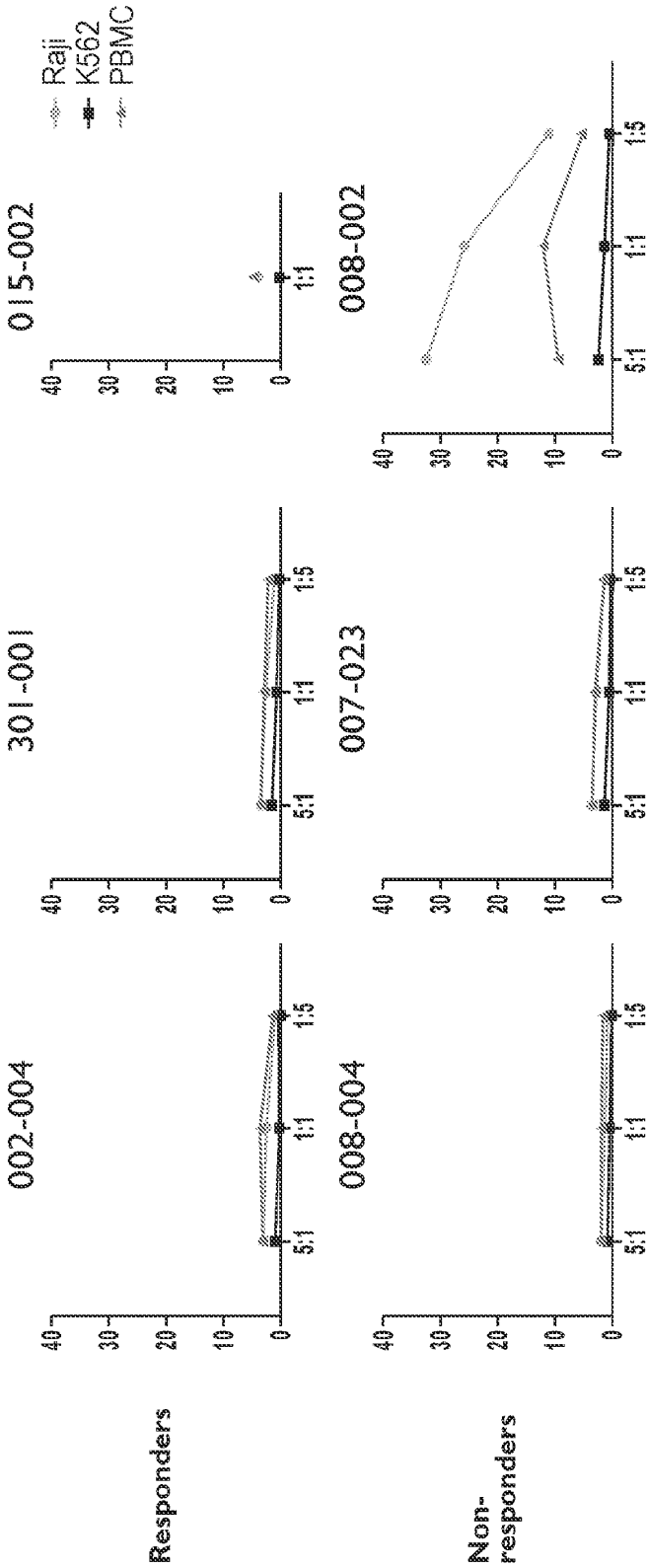


Figure 50

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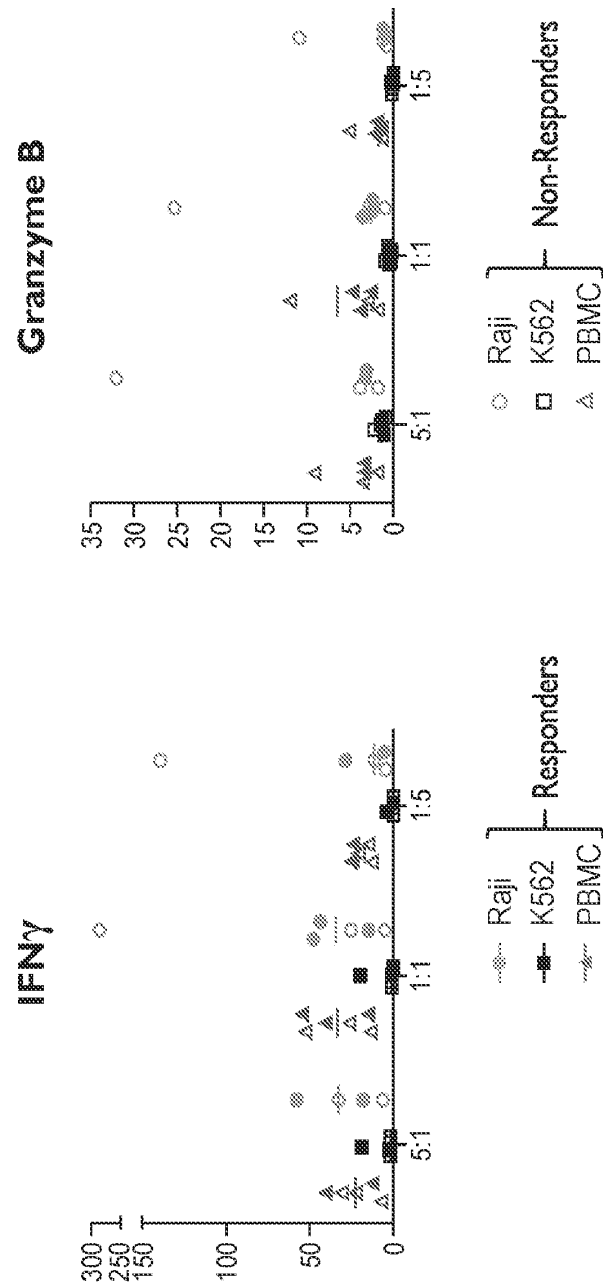


Figure 51

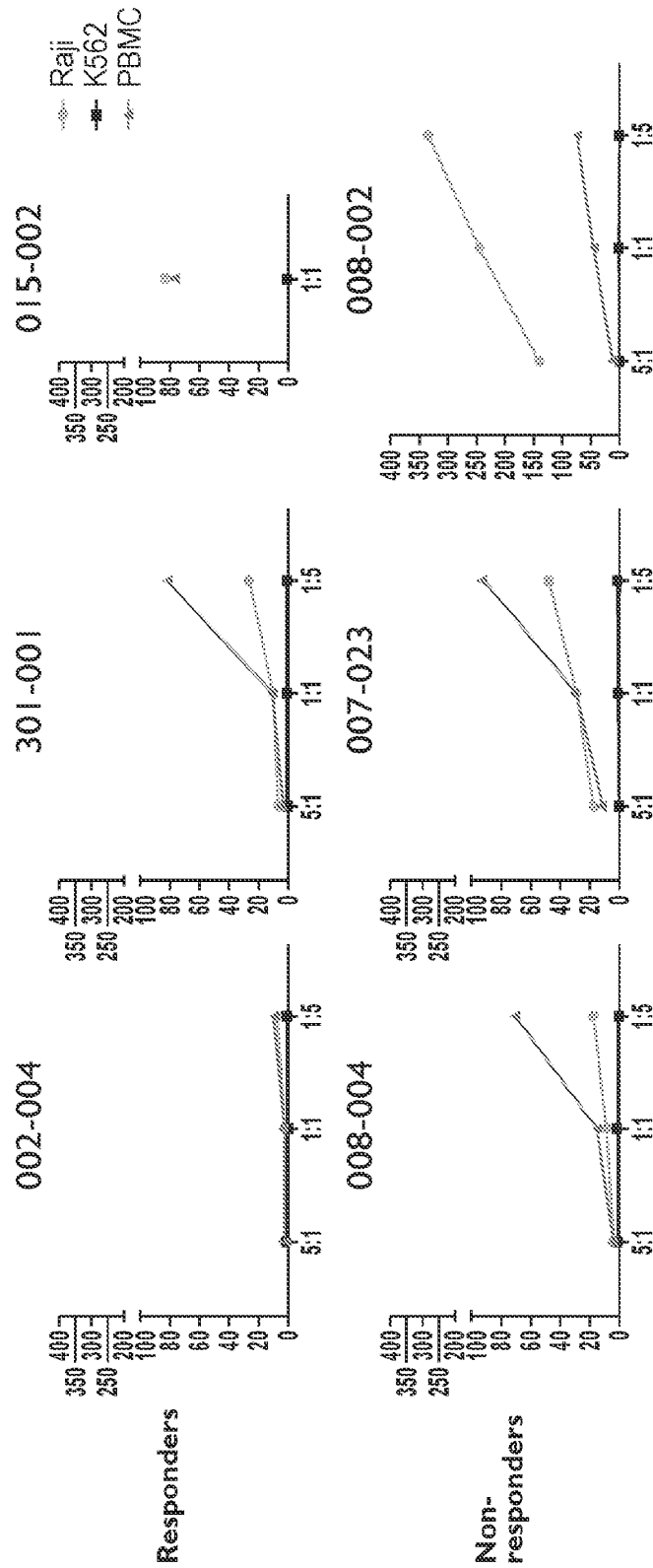


Figure 52

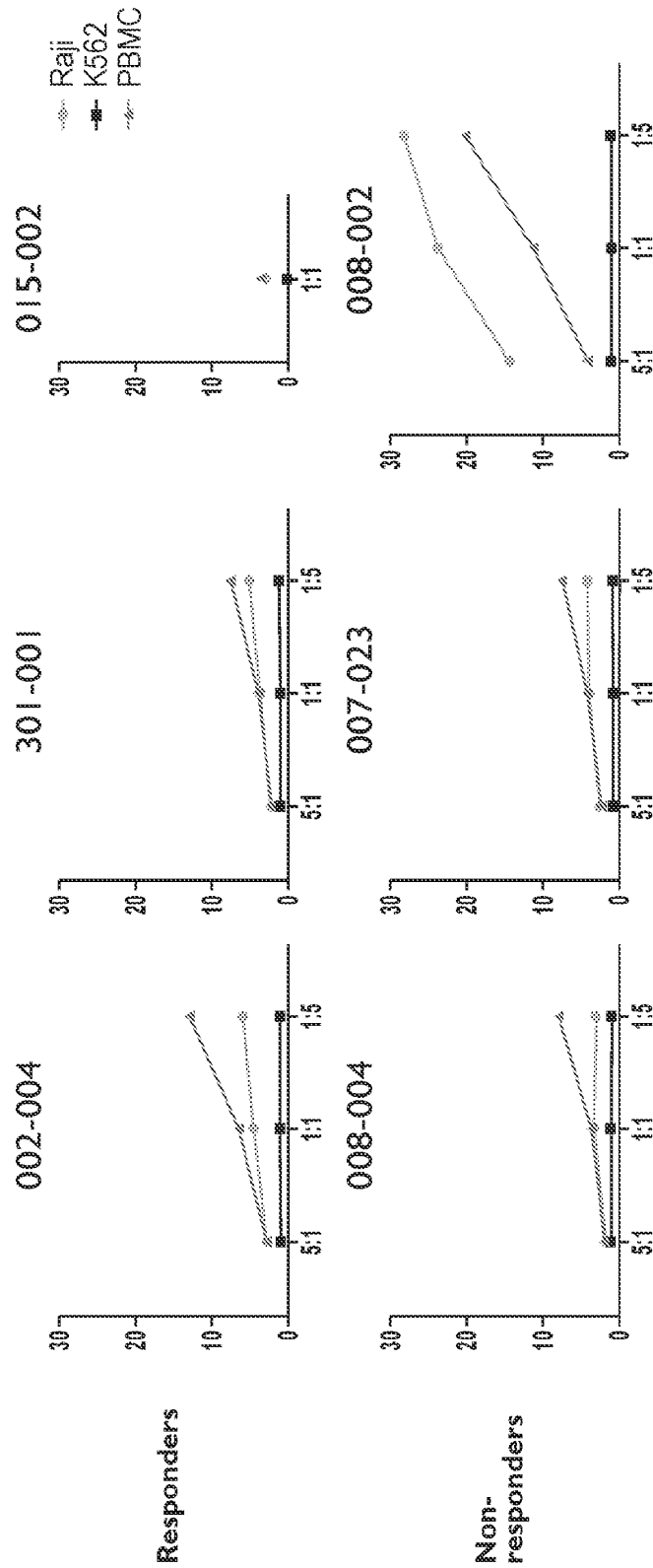


Figure 53

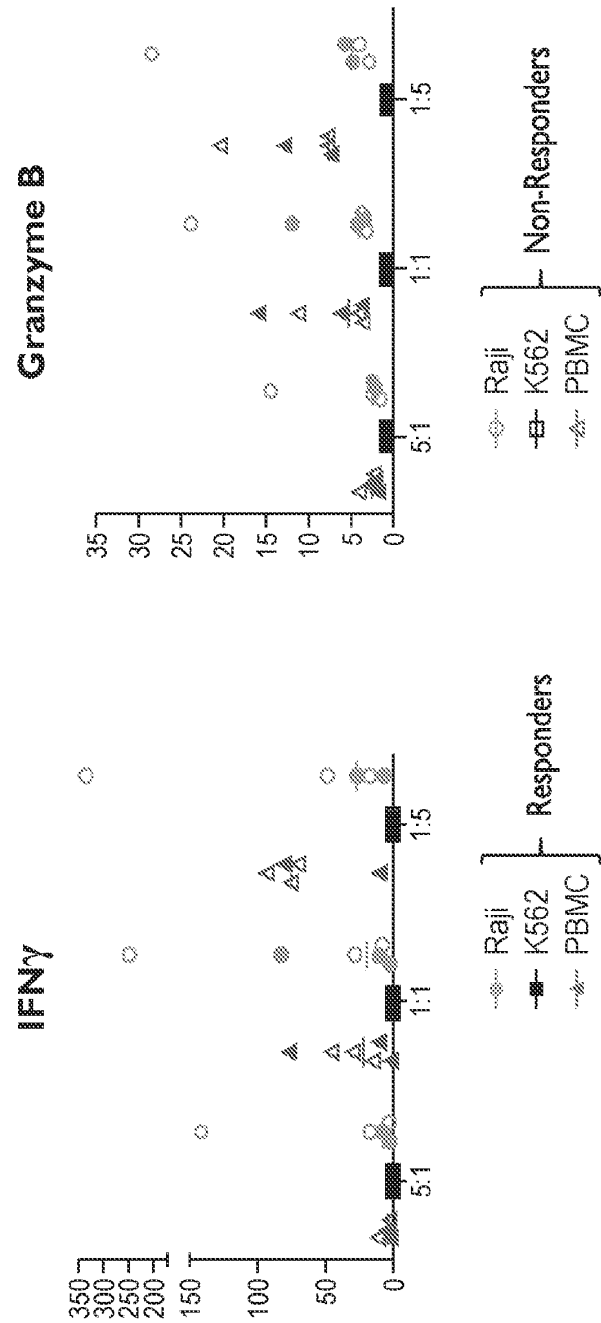


Figure 54

Cytokine	Number (Samples)	TIL:Target Ratio	Mean	Median	Minimum	Maximum
IFN γ	6	5:1	1039	174	53	3998
		1:1	855	269	42	3708
		1:5	481	61	23	1813
Granzyme B	6	5:1	3296	1877	738	11011
		1:1	2569	1527	568	8721
		1:5	1167	683	317	3745

Figure 55

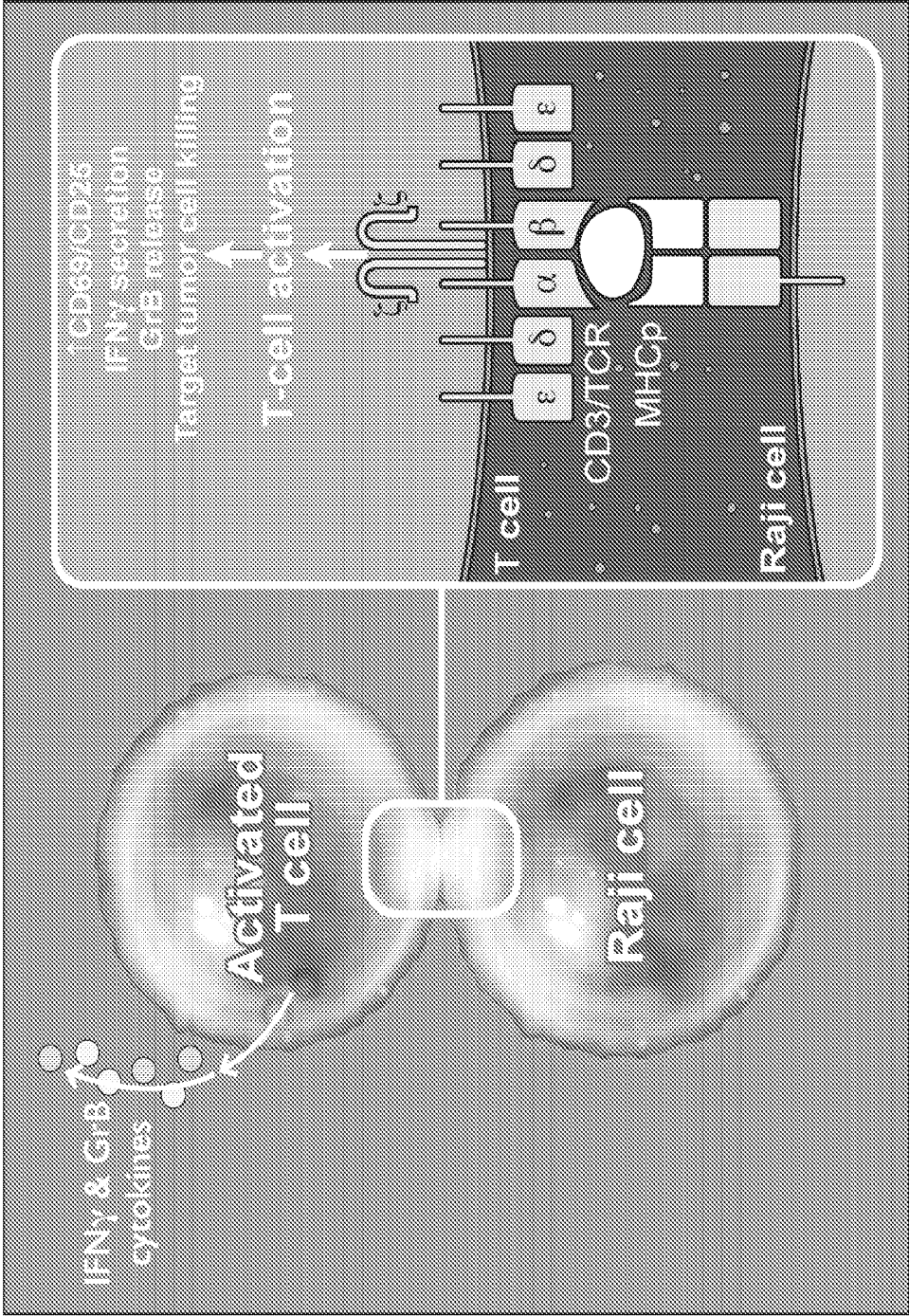


Figure 56

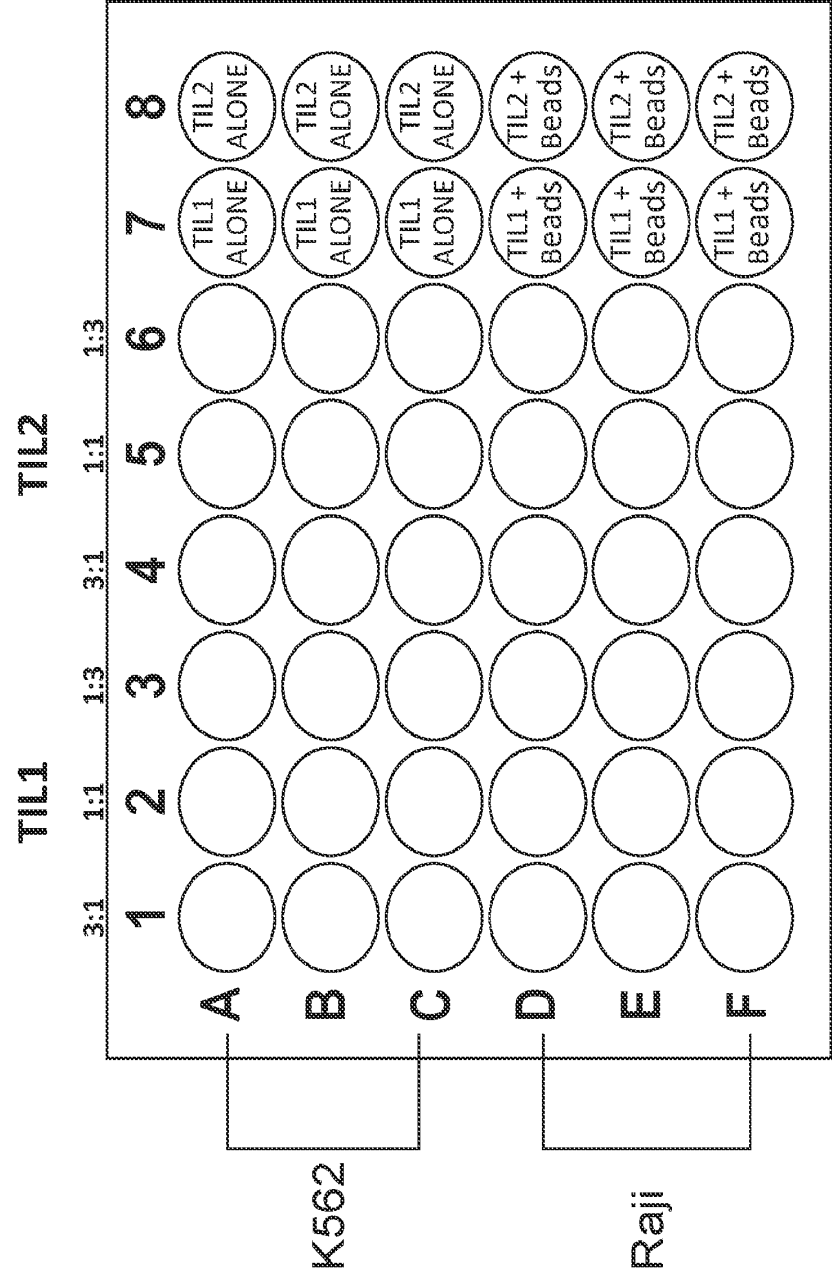


Figure 57

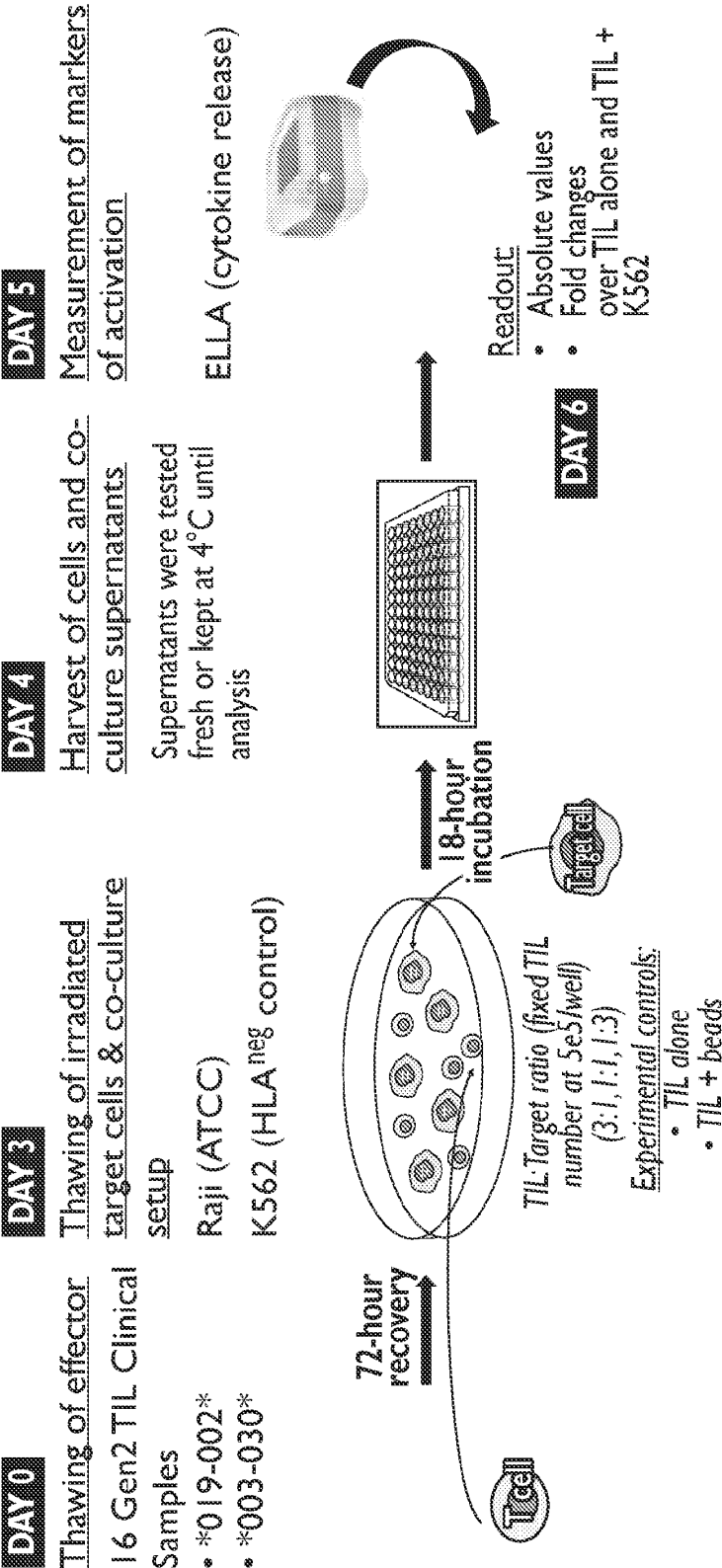
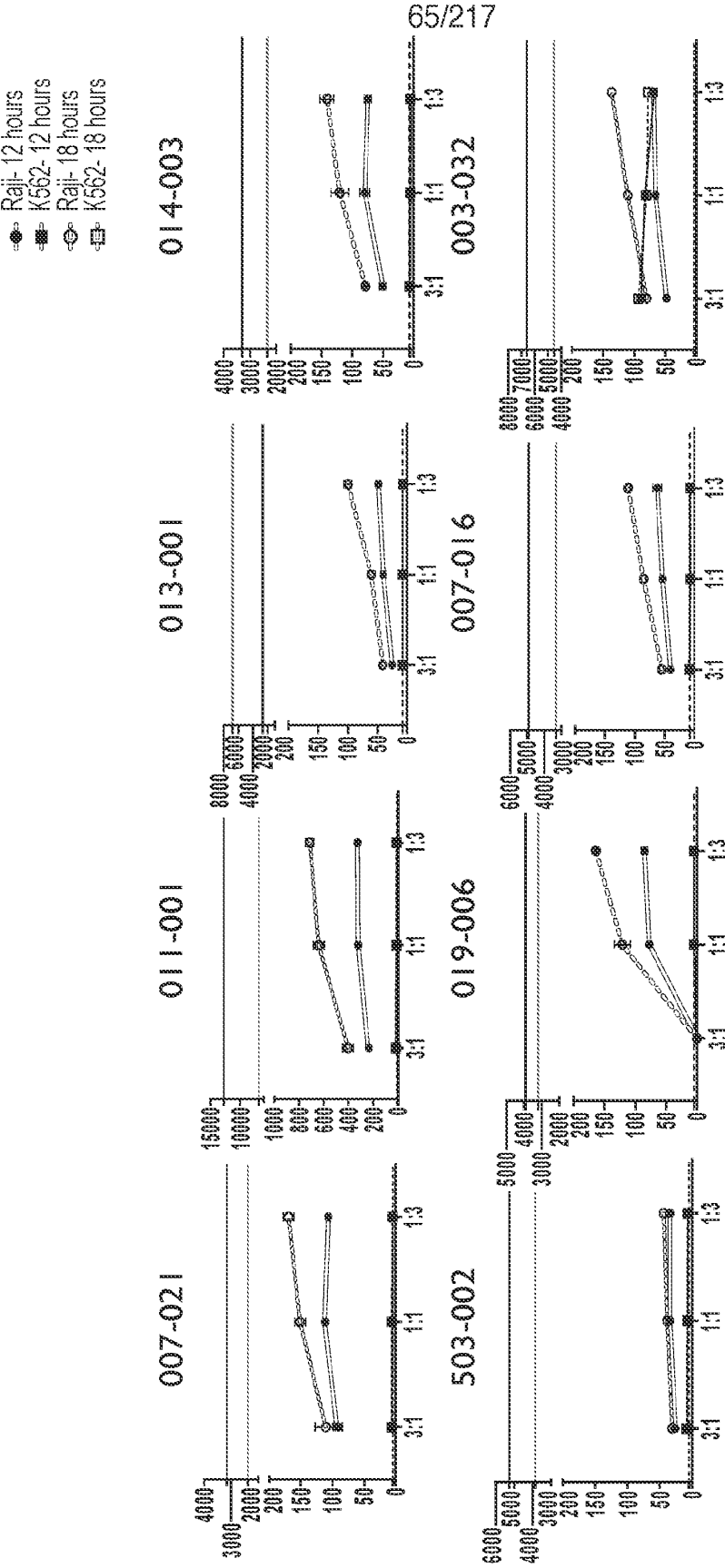
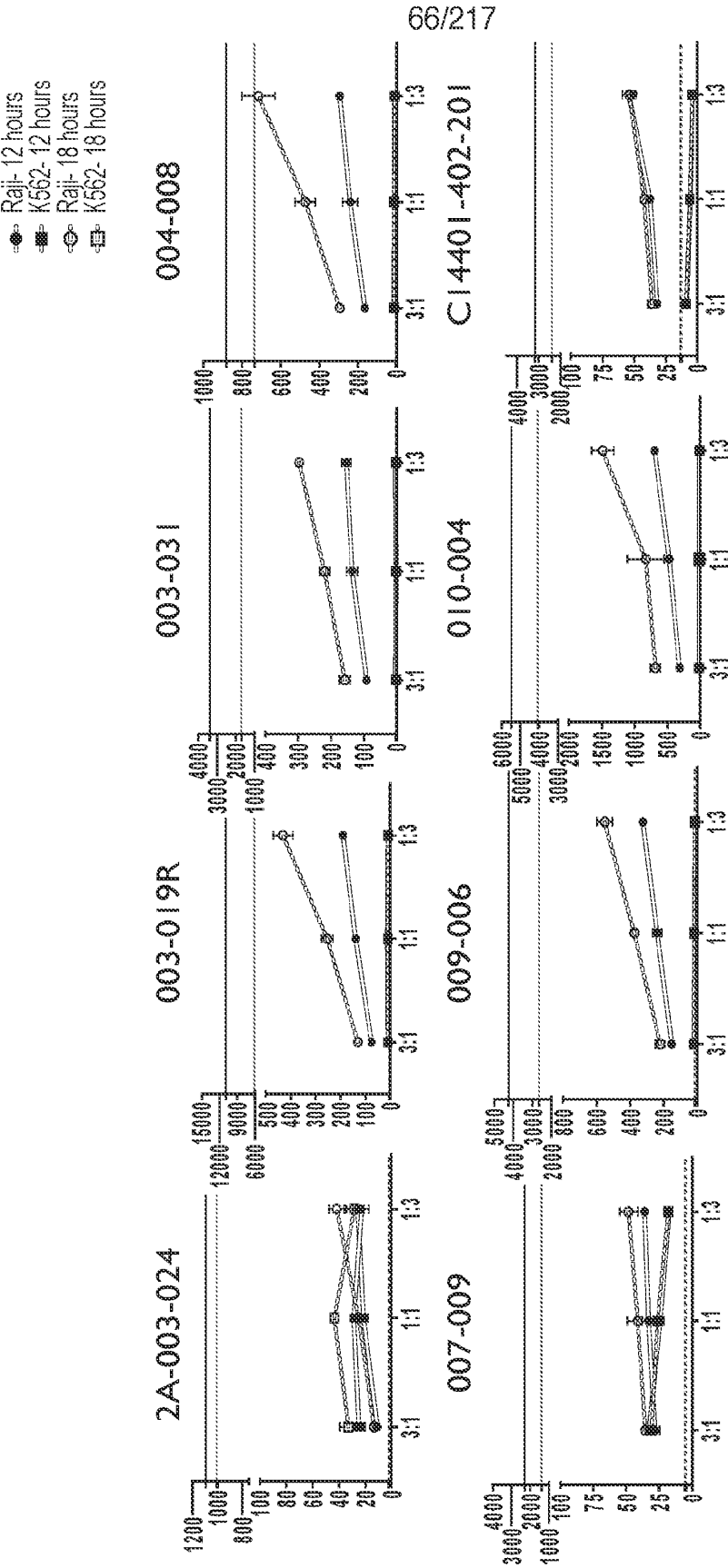


Figure 58



Solid gray line = 12 hours: α CD3/ α CD28/ α 41BB beads
Dotted gray line = 12 hours unstimulated TIL
Solid black line = 18 hours: α CD3/ α CD28/ α 41BB beads
Dotted black line = 18 hours unstimulated TIL

Figure 59



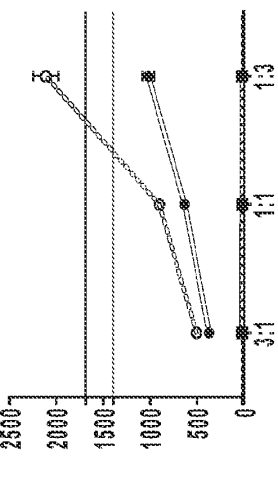
Solid gray line = 12 hours: α CD3/ α CD28/ α 41BB beads
Dotted gray line = 12 hours unstimulated TIL
Solid black line = 18 hours: α CD3/ α CD28/ α 41BB beads
Dotted black line = 18 hours unstimulated TIL

Figure 60

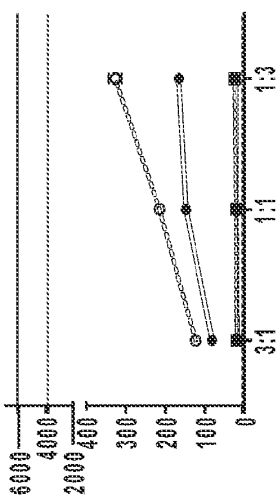
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- Raji- 12 hours
- K562- 12 hours
- Raji- 18 hours
- K562- 18 hours

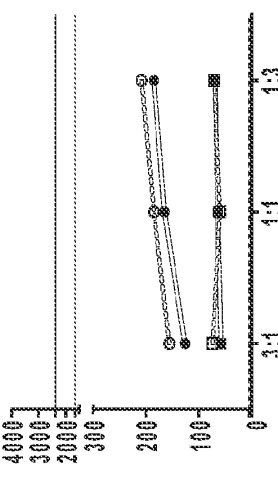
015-001



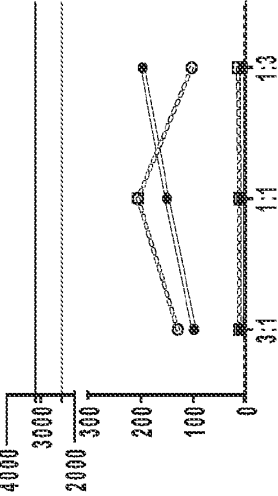
019-004



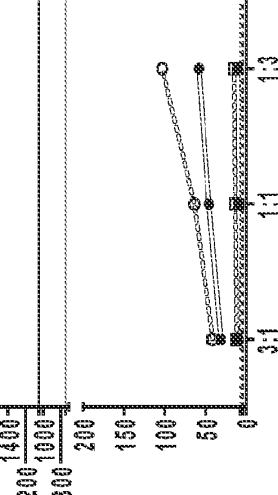
022-001



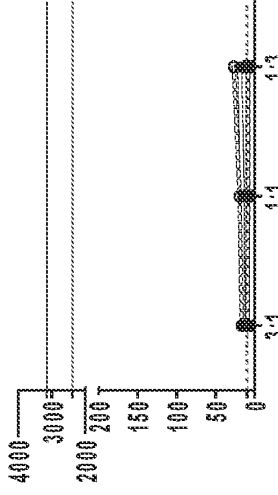
2A-007-013



2A-014-002



CI4401-505-001



Solid gray line = 12 hours: α CD3/ α CD28/ α 41BB beads
Dotted gray line = 12 hours unstimulated TIL
Solid black line = 18 hours: α CD3/ α CD28/ α 41BB beads
Dotted black line = 18 hours unstimulated TIL

Figure 61

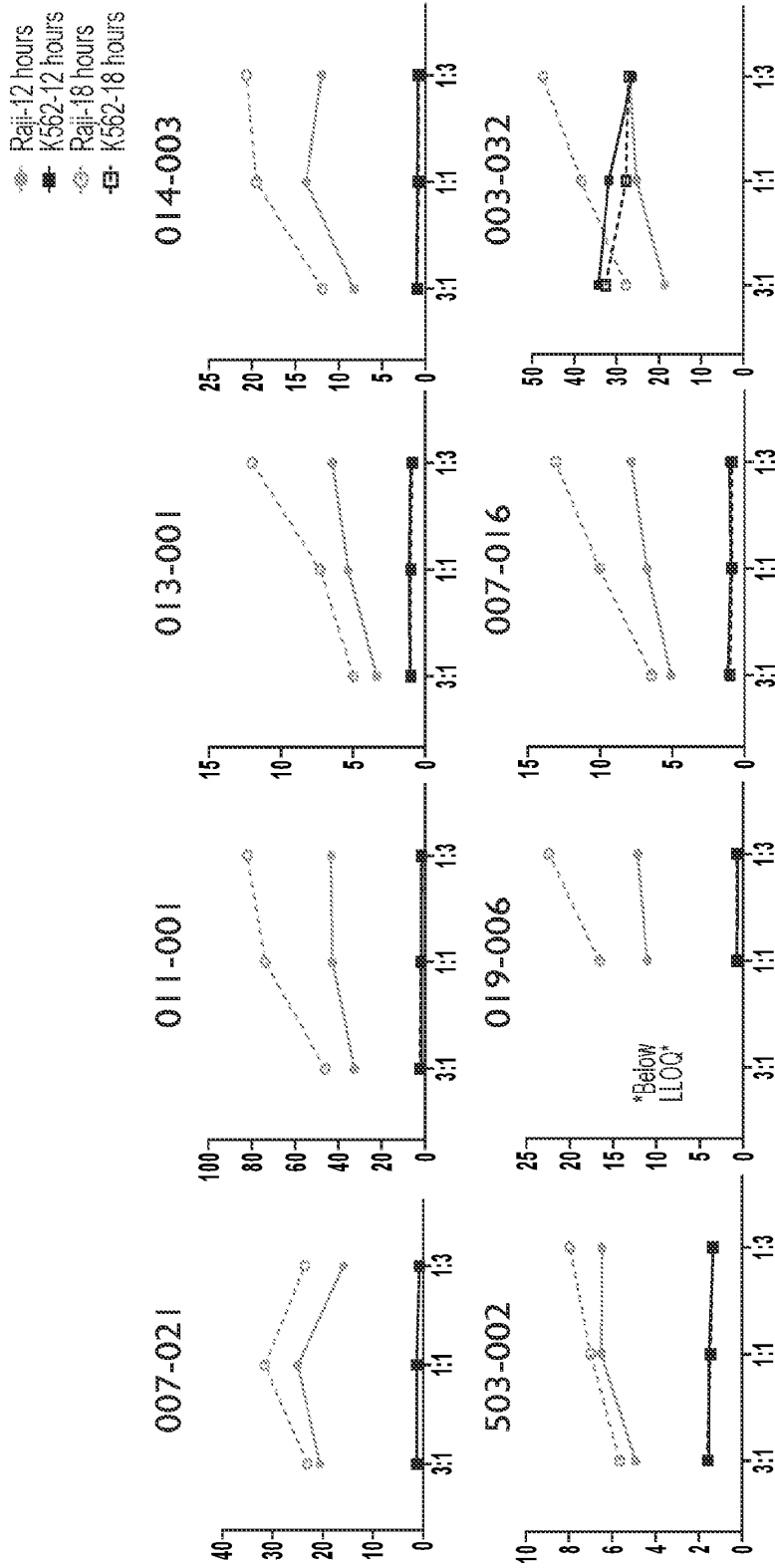


Figure 62

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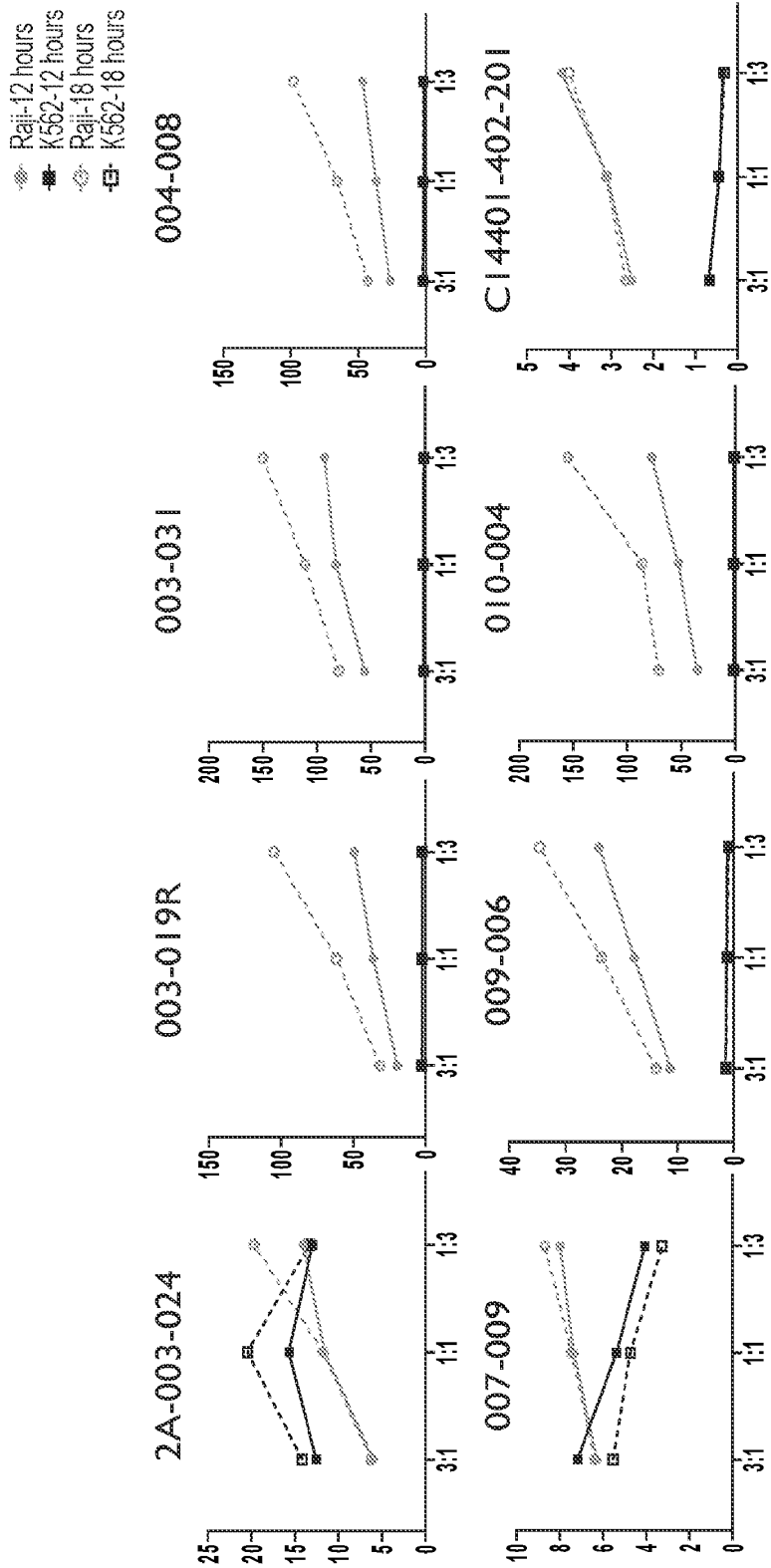


Figure 63

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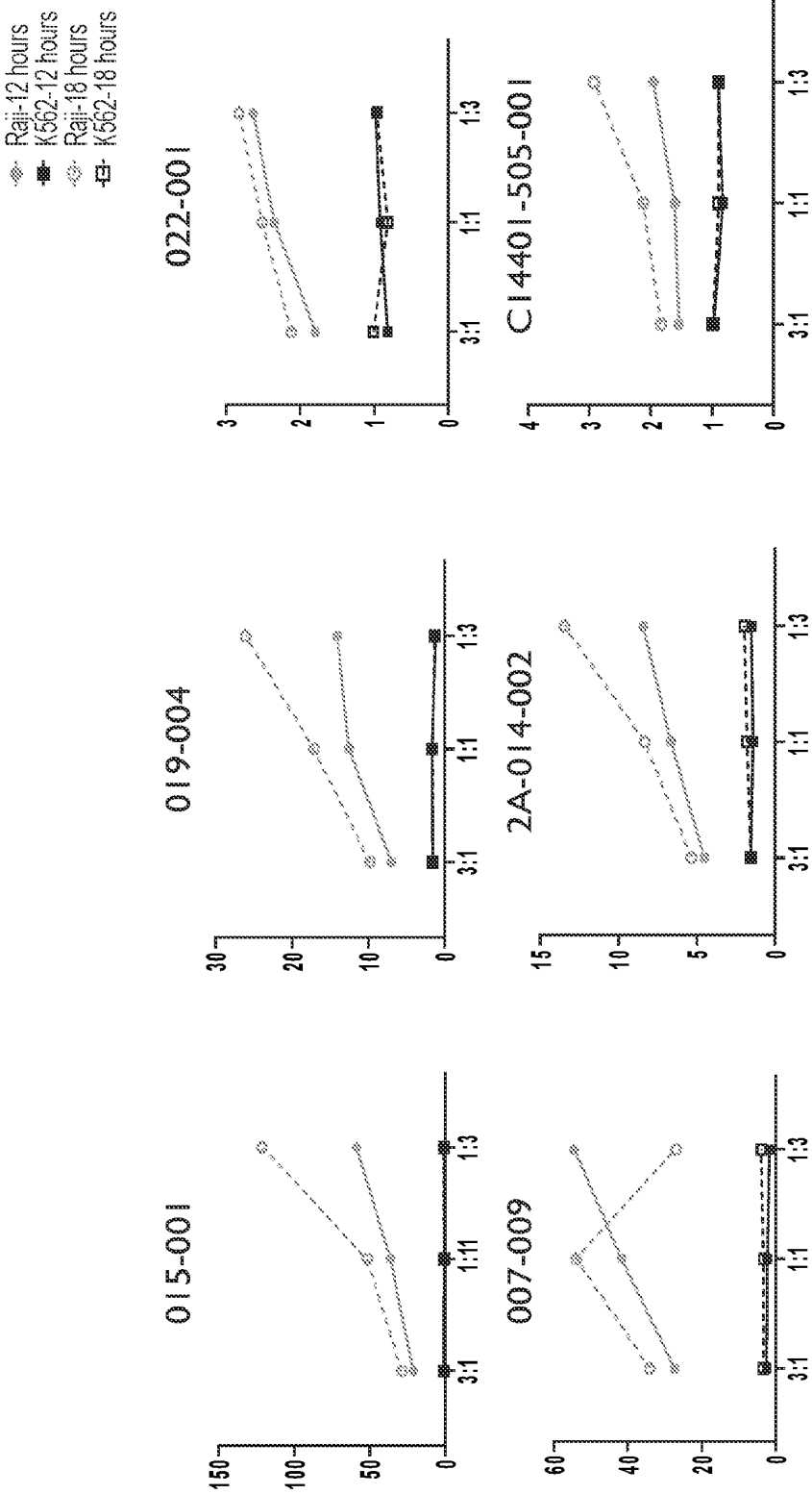


Figure 64

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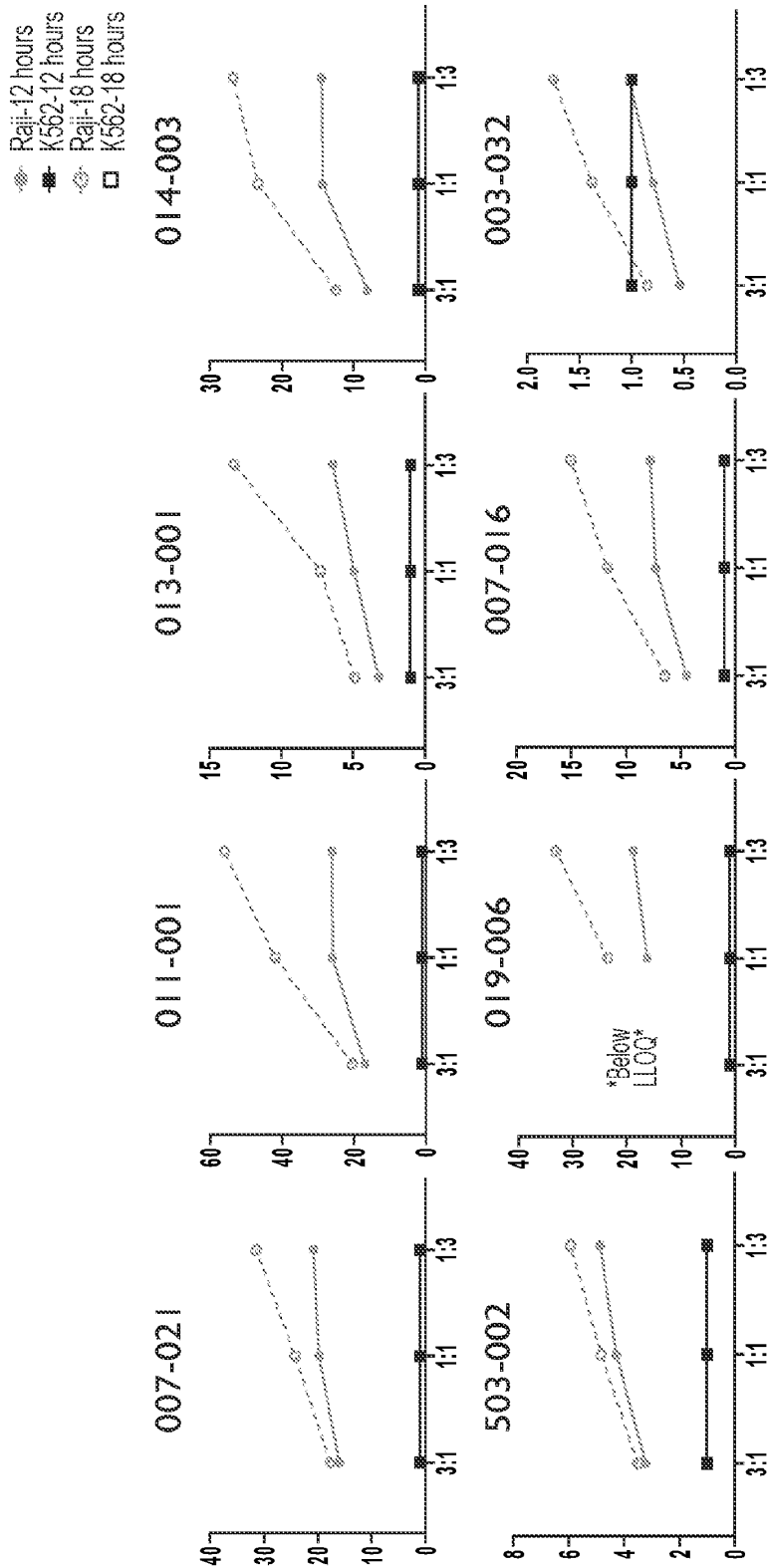


Figure 65

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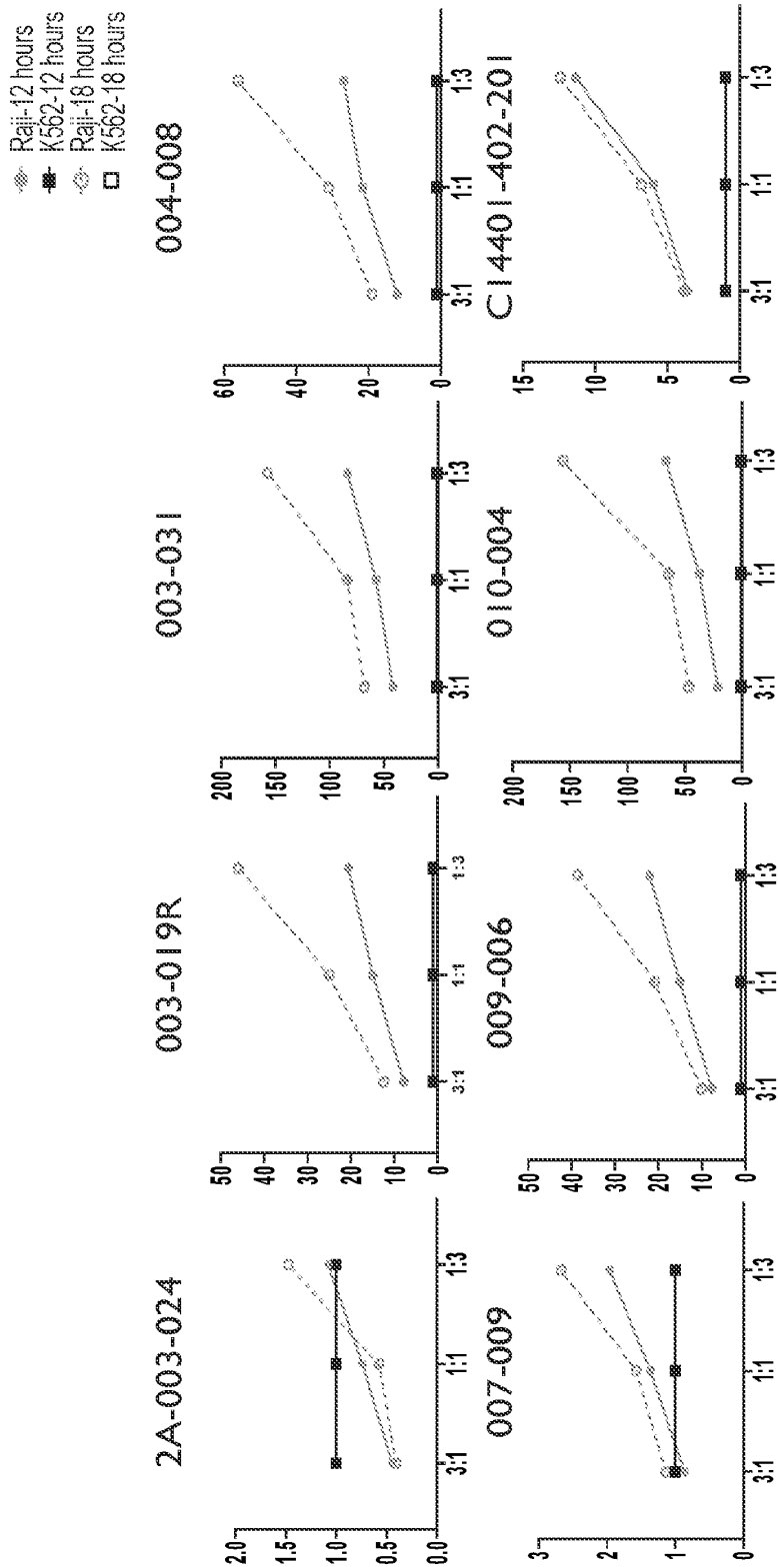


Figure 66

73/217

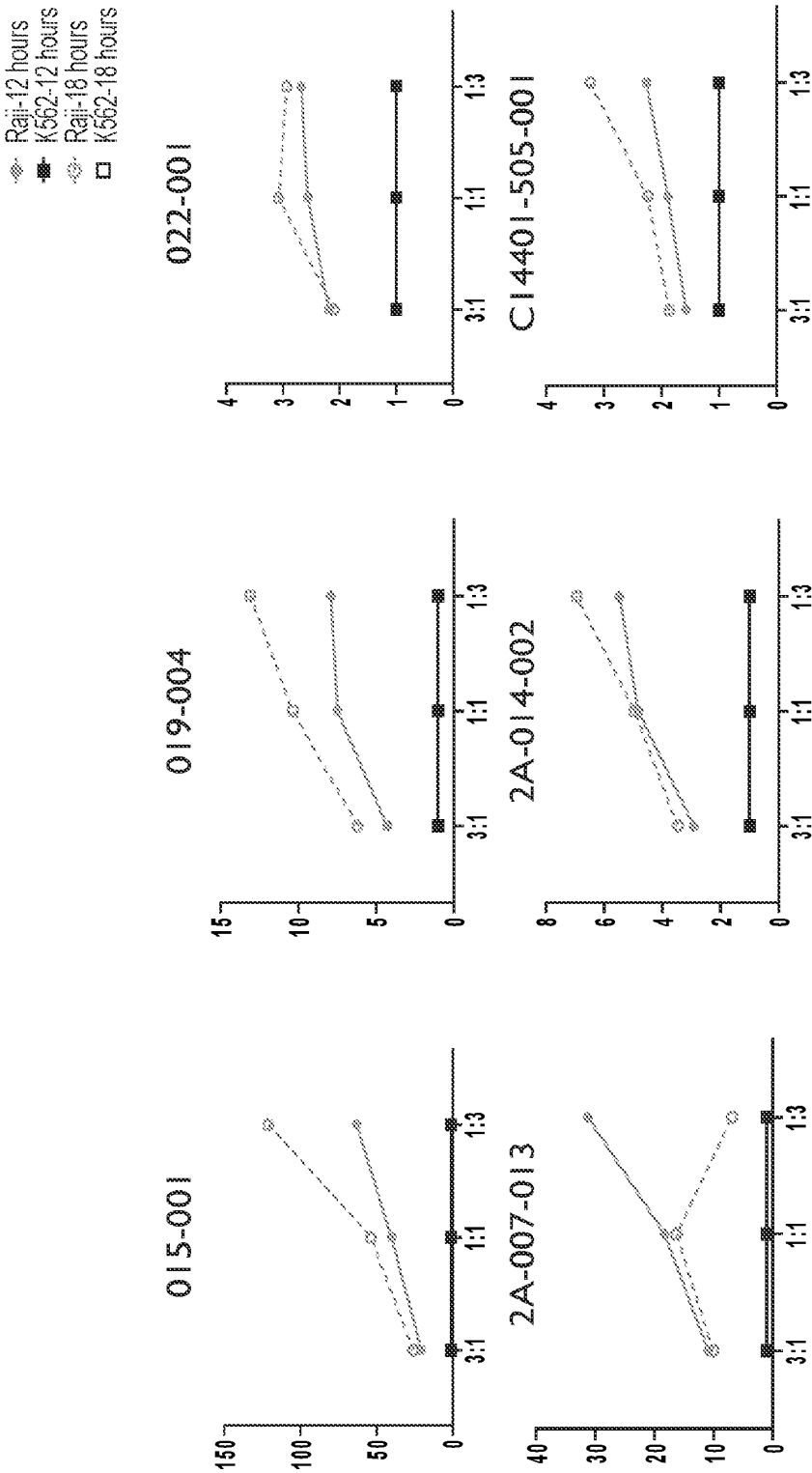


Figure 67

74/217

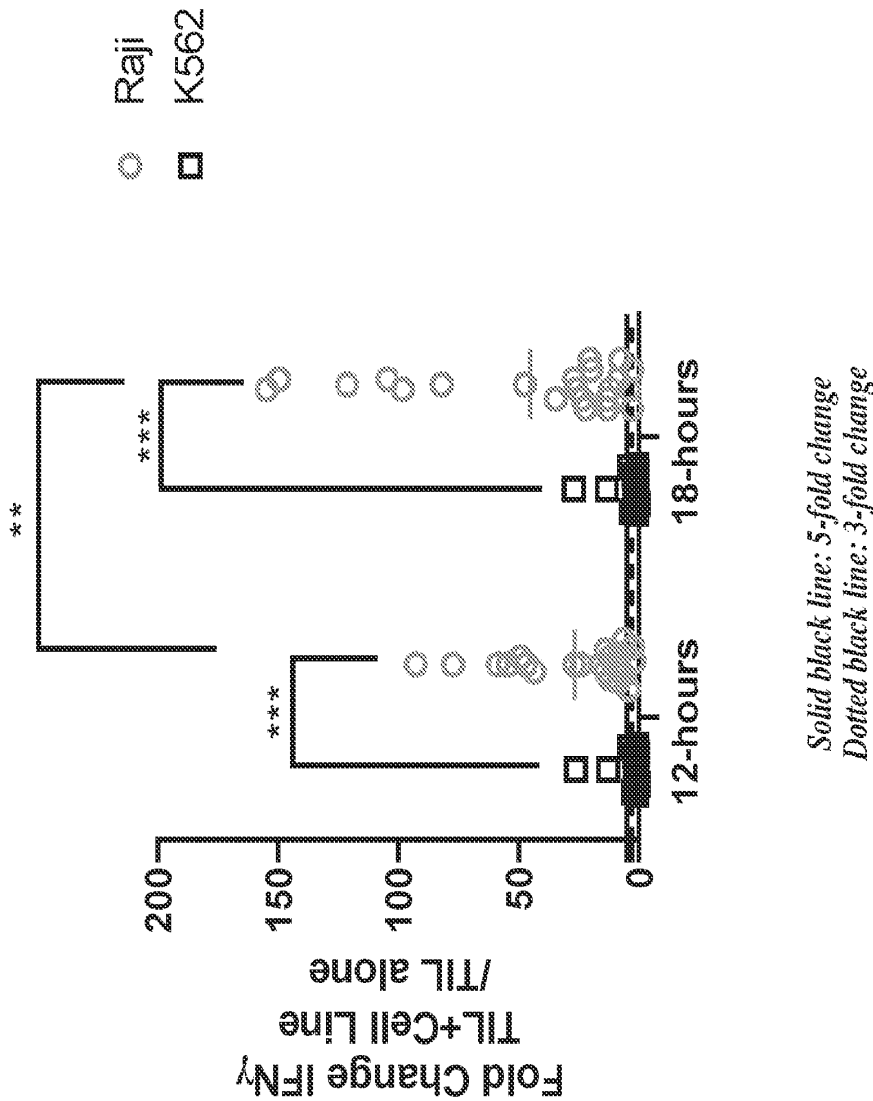


Figure 68

75/217

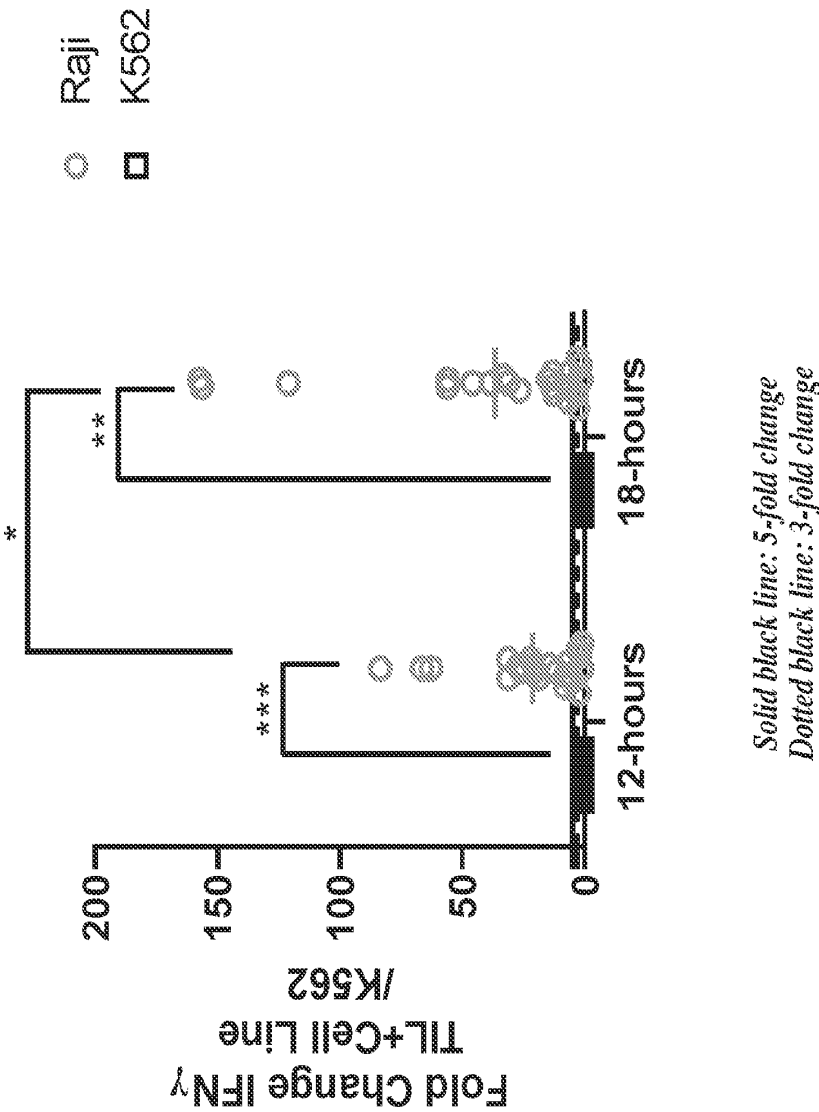


Figure 69

76/217

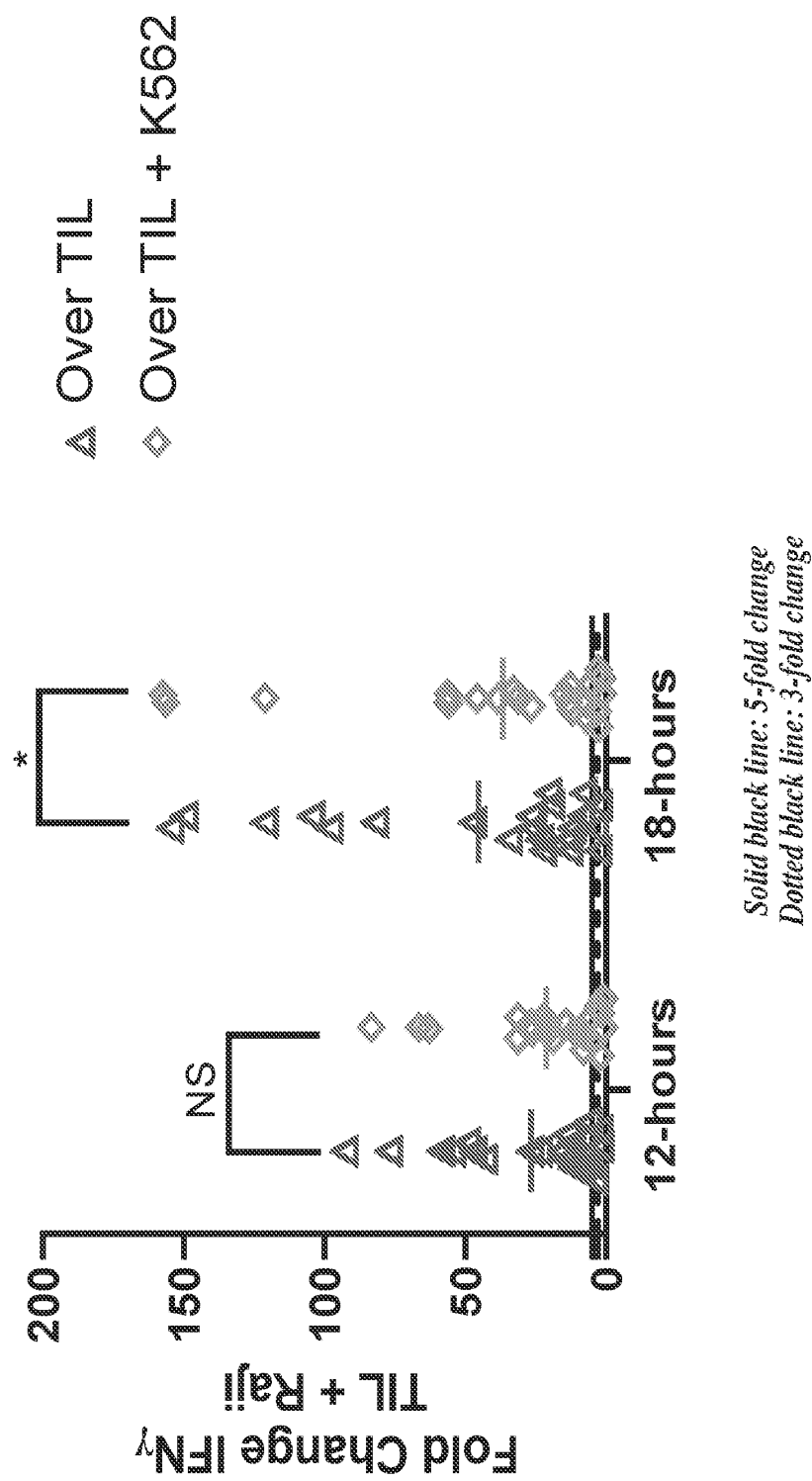


Figure 70

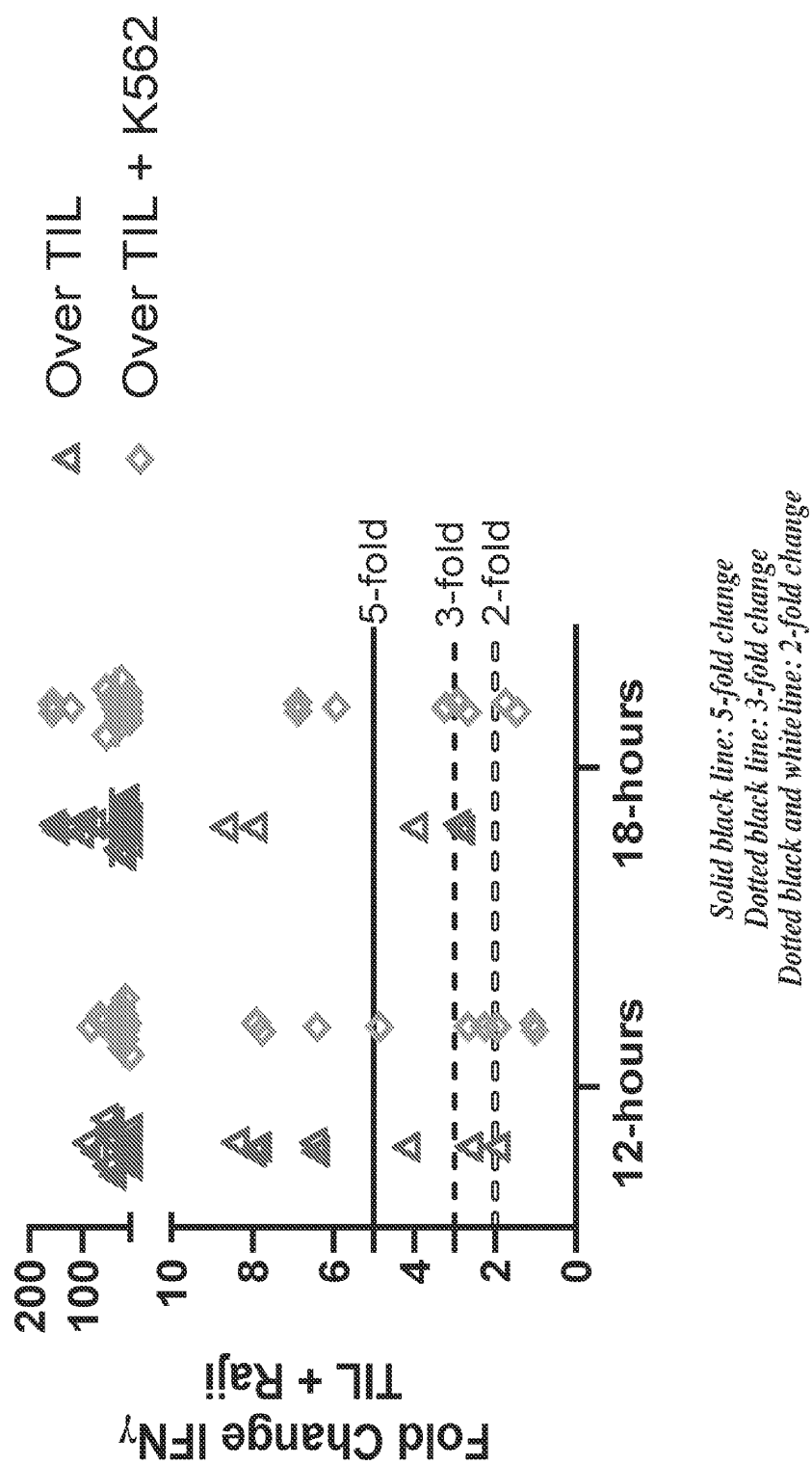
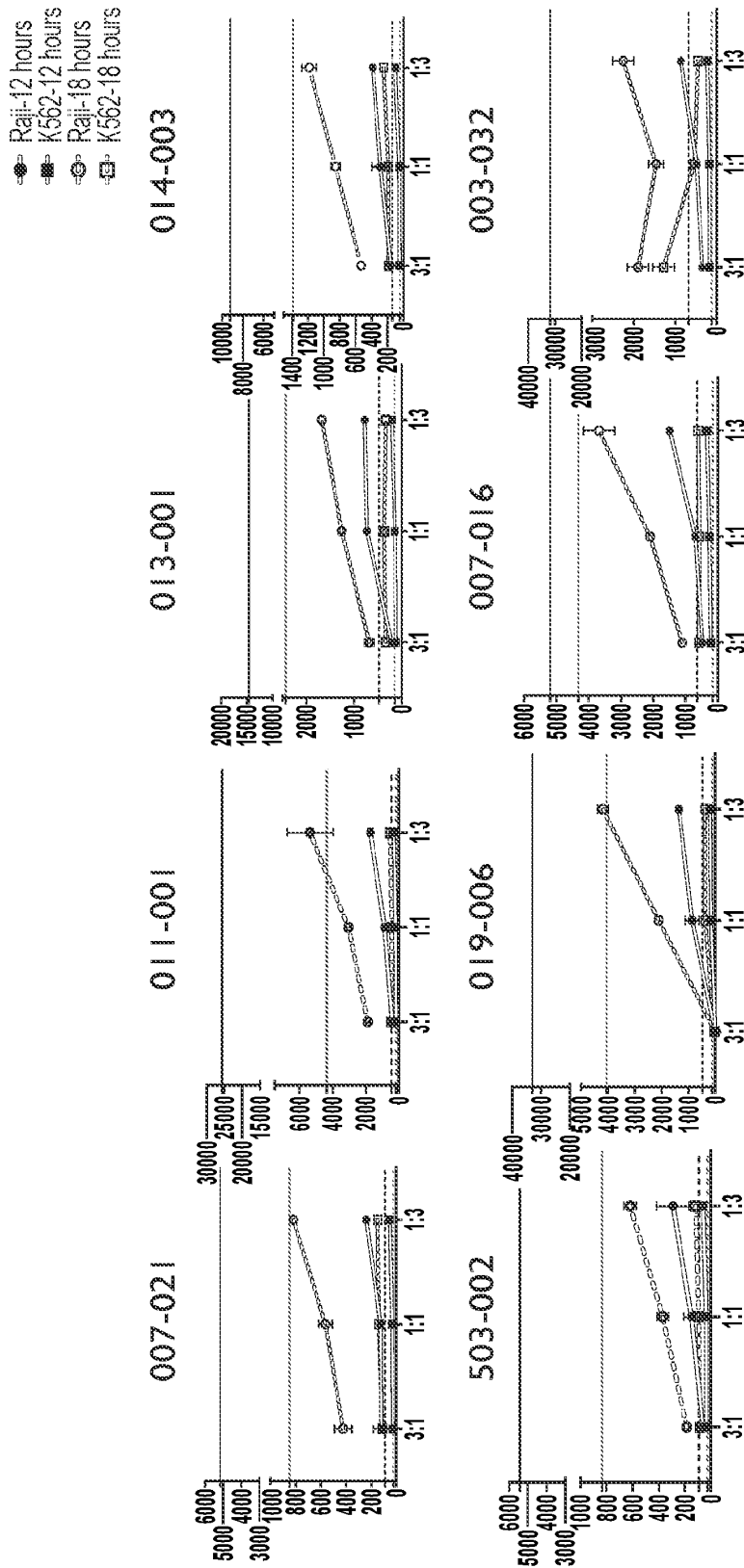


Figure 71

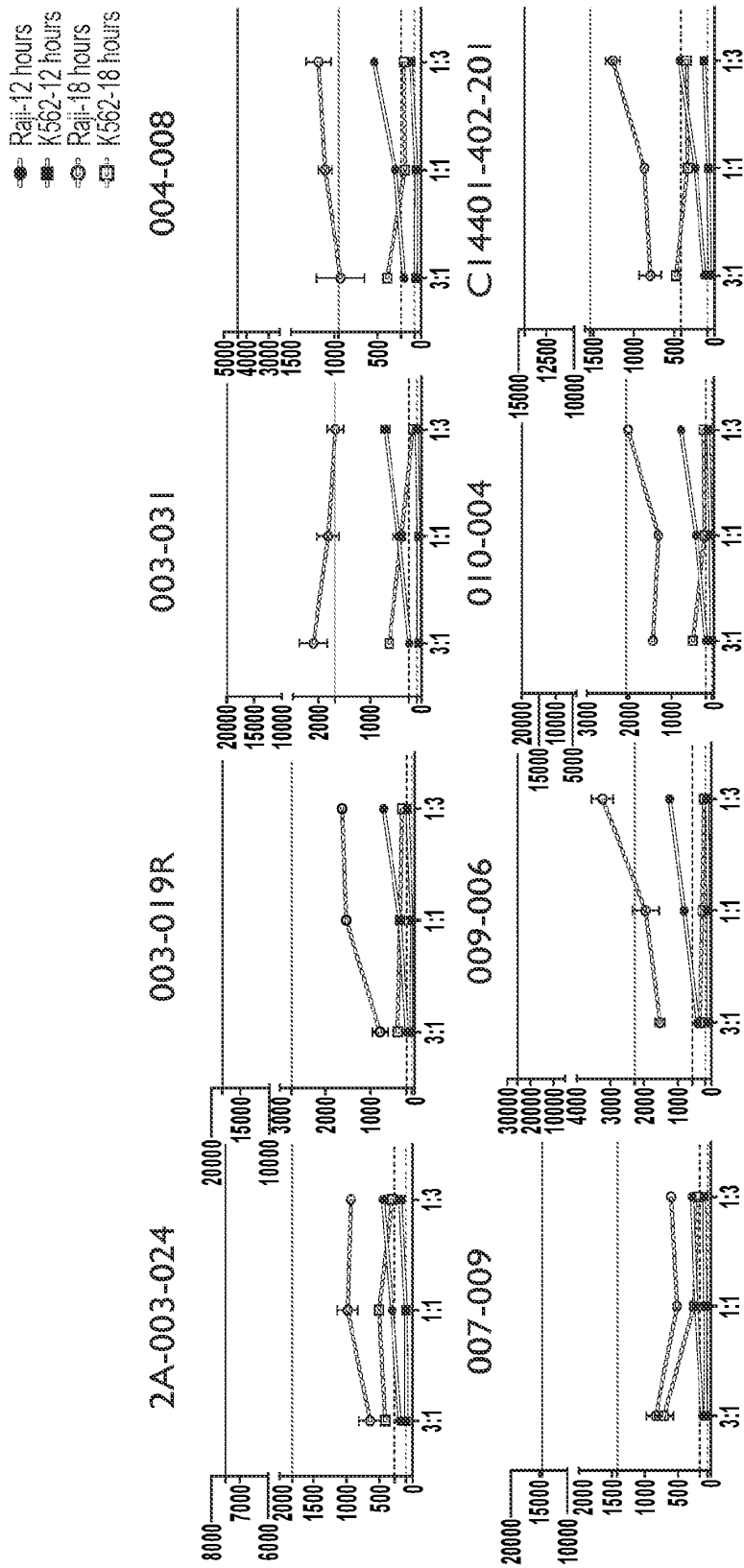
78/217



Solid gray line = 12 hours: α CD3/ α CD28/ α 41BB beads
Dotted gray line = 12 hours unstimulated TIL
Solid black line = 18 hours: α CD3/ α CD28/ α 41BB beads
Dotted black line = 18 hours unstimulated TIL

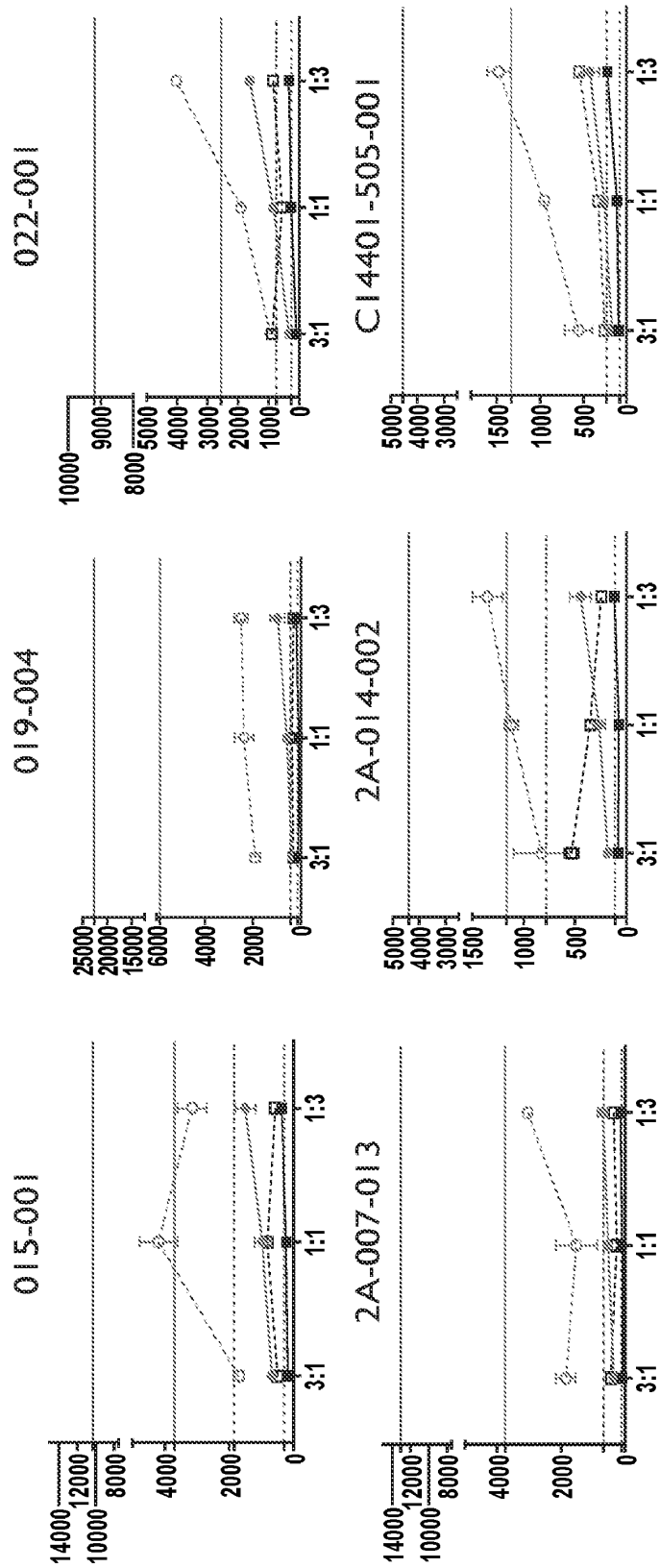
Figure 72

79/217



Solid gray line = 12 hours: α CD3/ α CD28/ α 41BB beads
Dotted gray line = 12 hours unstimulated TIL
Solid black line = 18 hours: α CD3/ α CD28/ α 41BB beads
Dotted black line = 18 hours unstimulated TIL

Figure 73



Solid gray line = 12 hours; α CD3/ α CD28/ α 41BB beads
Dotted gray line = 12 hours unstimulated TIL
Solid black line = 18 hours; α CD3/ α CD28/ α 41BB beads
Dotted black line = 18 hours unstimulated TIL

Figure 74

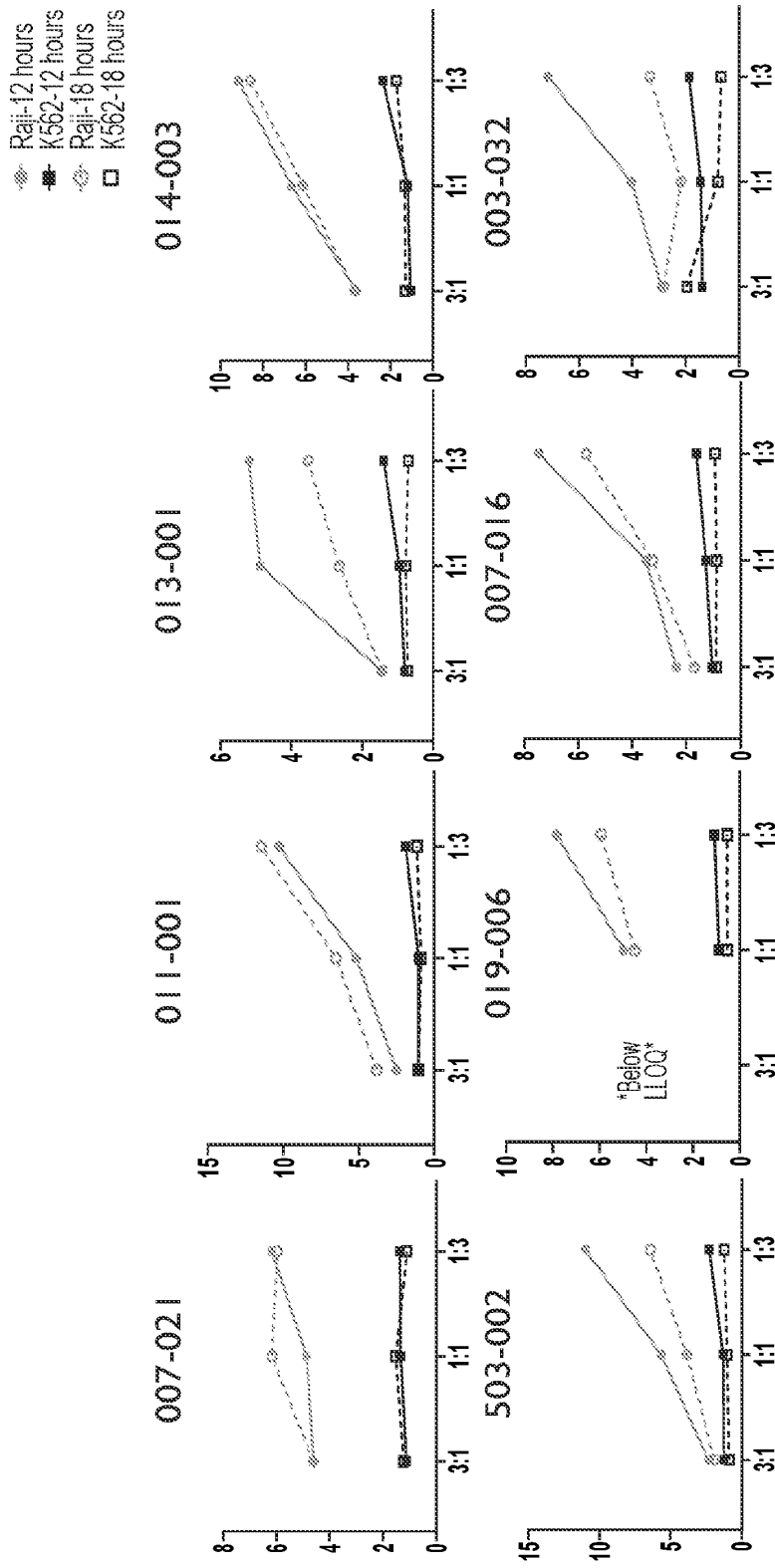


Figure 75

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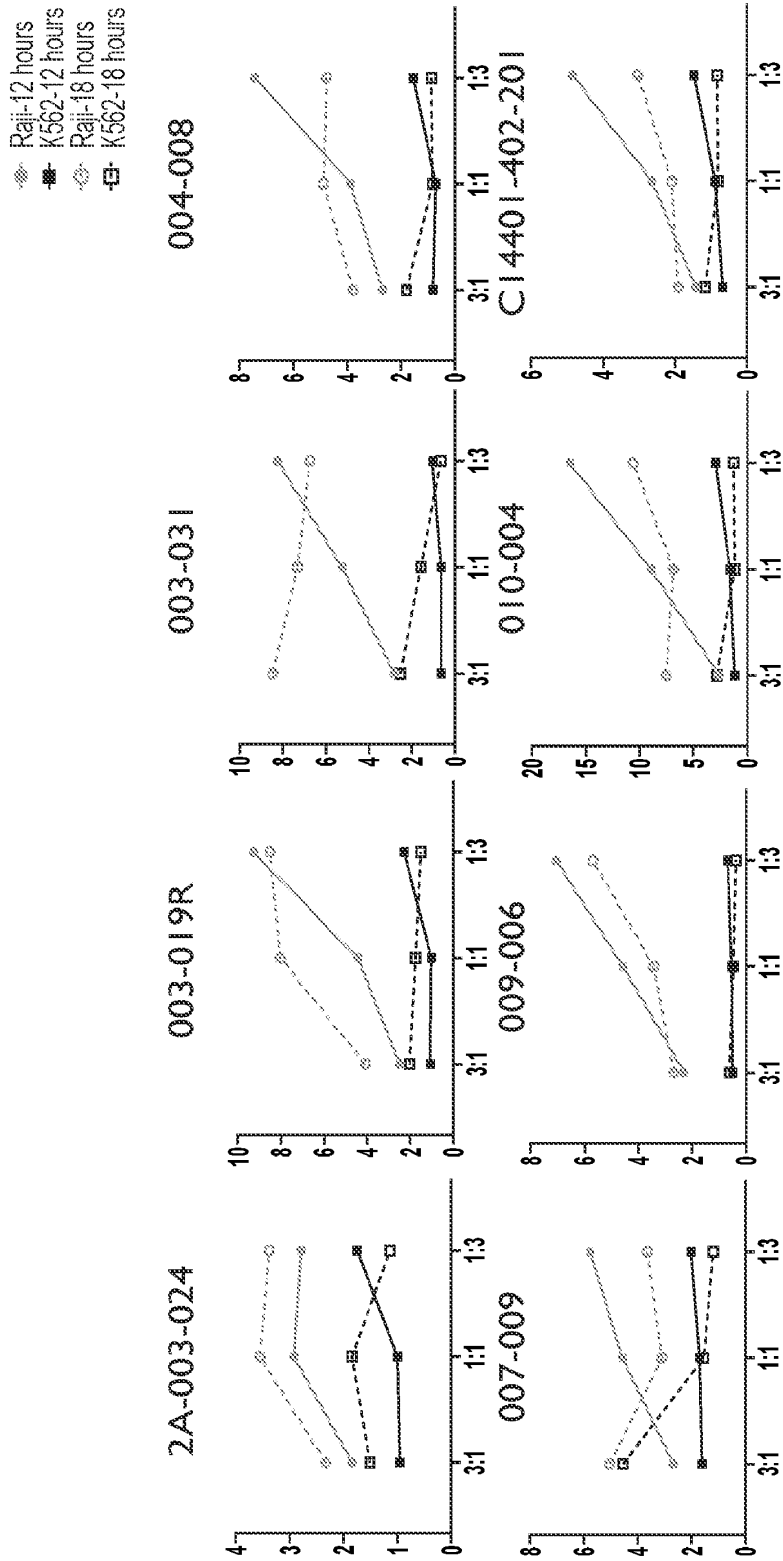


Figure 76

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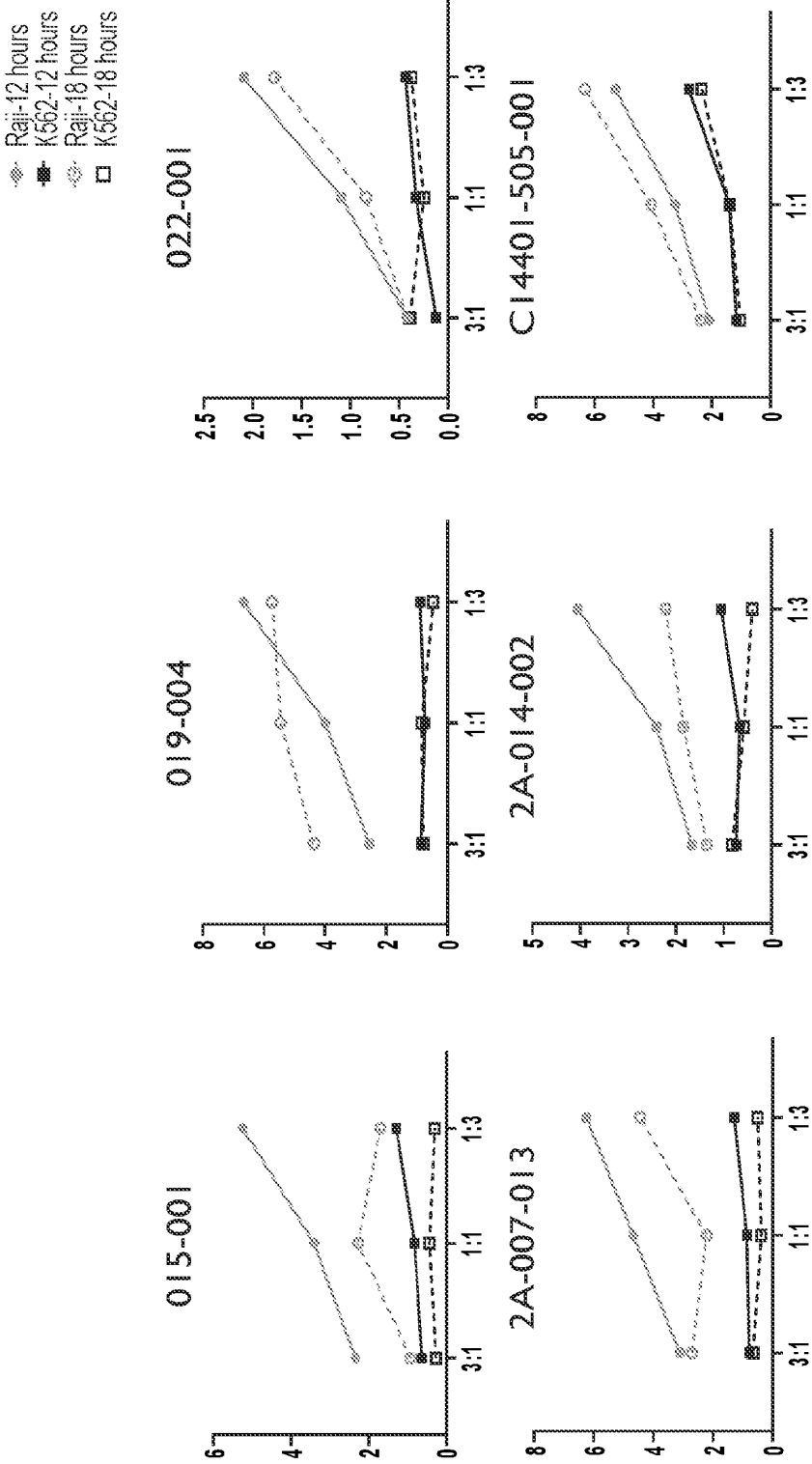


Figure 77

84/217

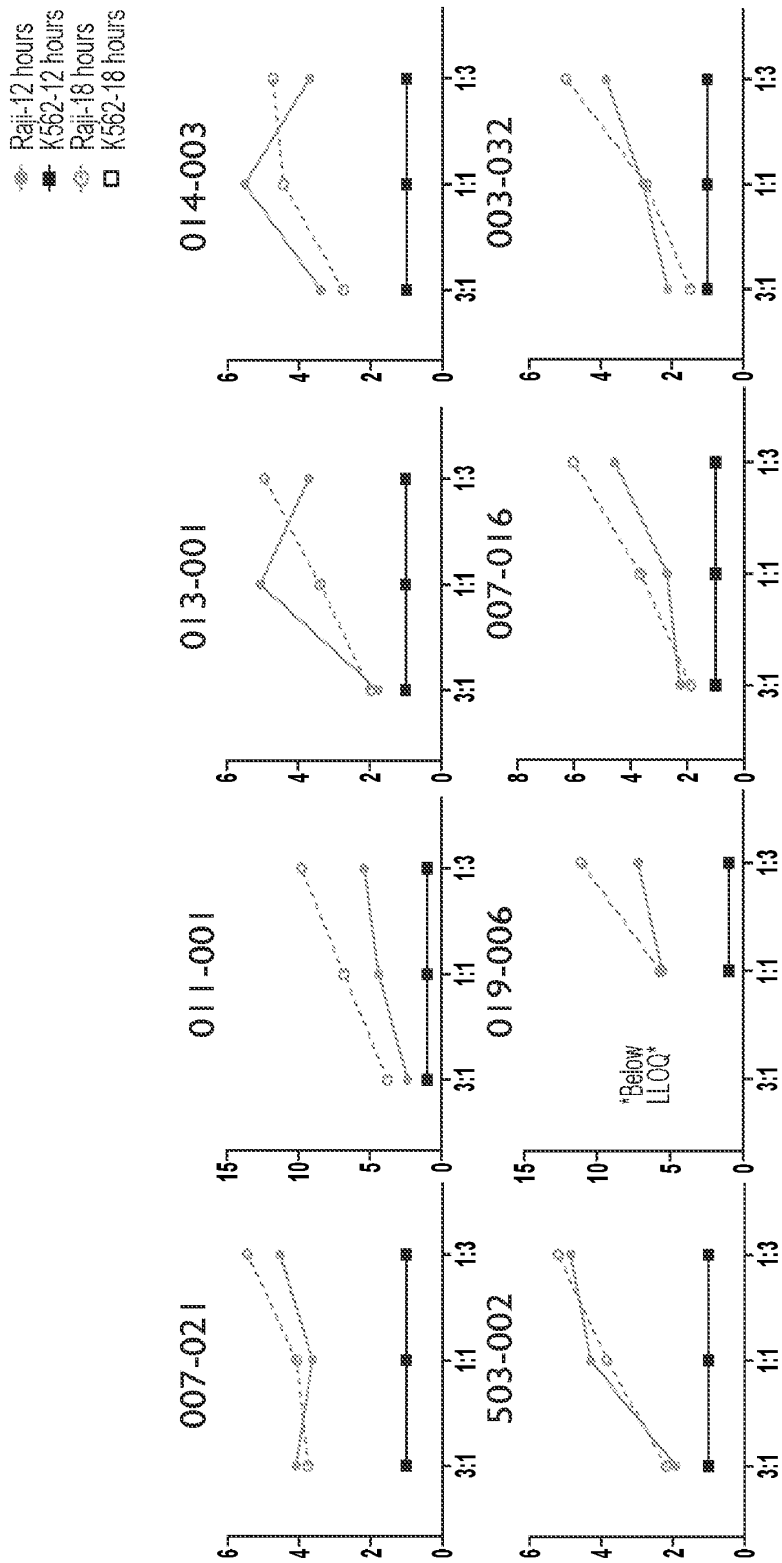


Figure 78

85/217

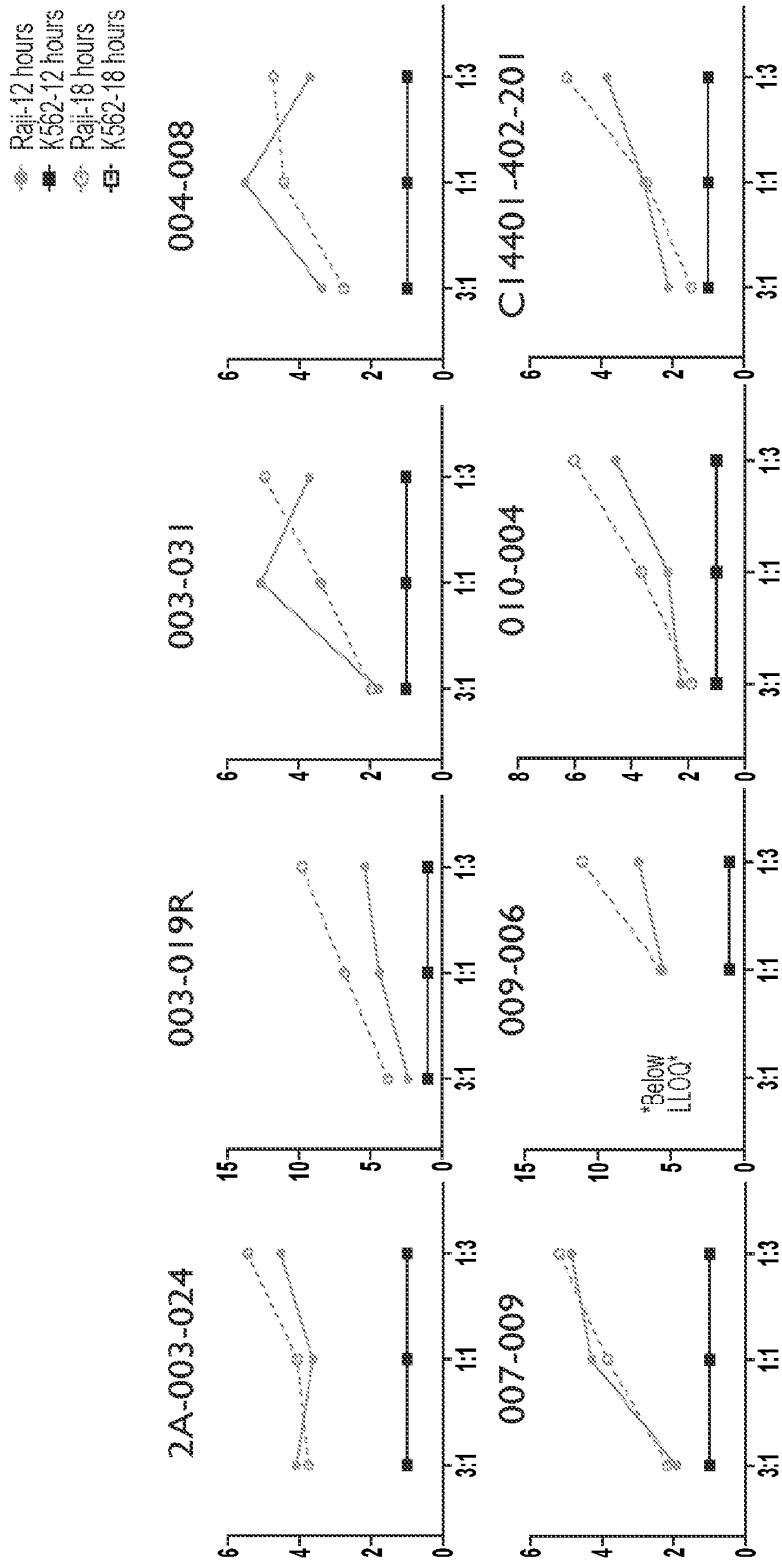


Figure 79

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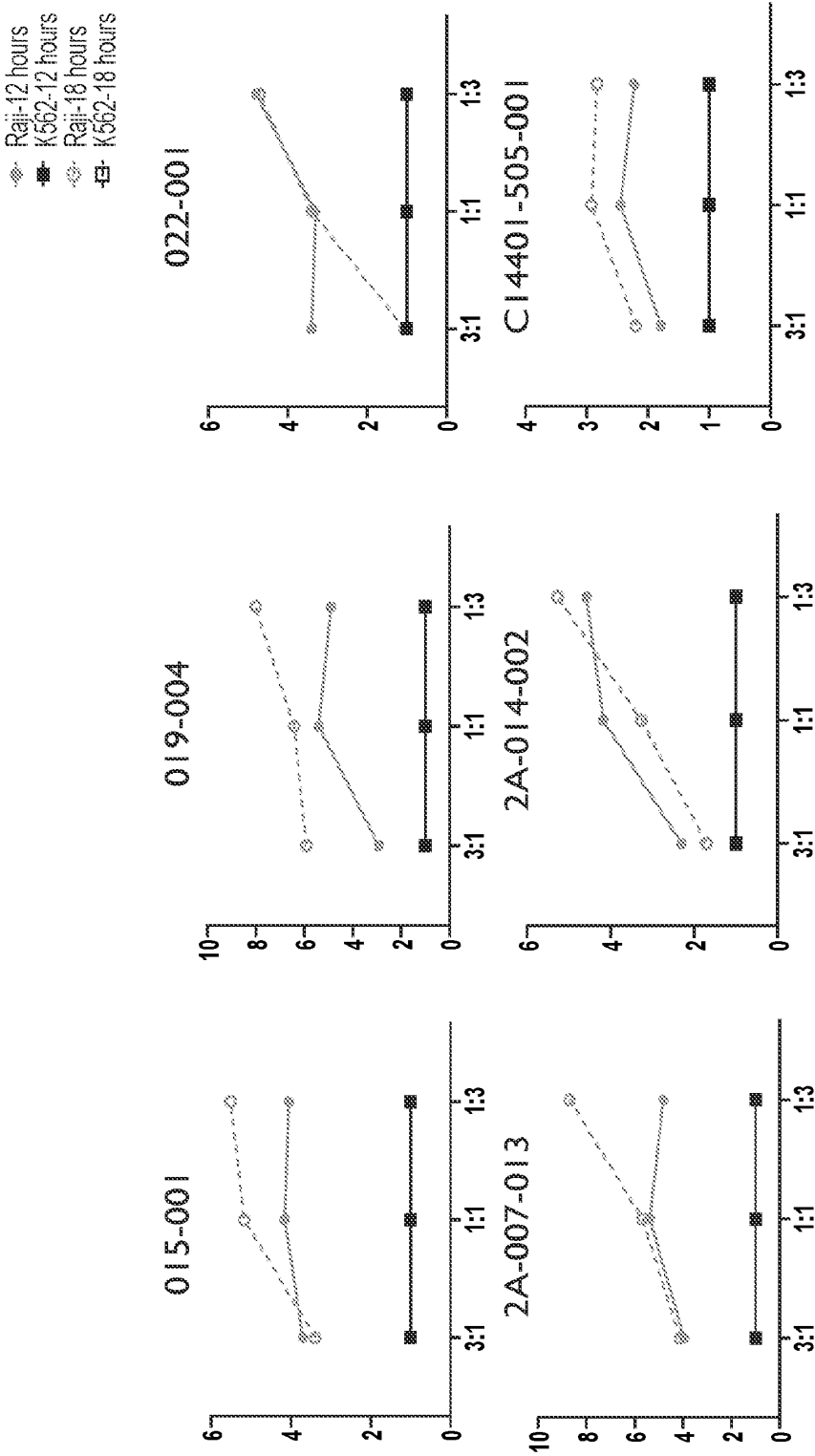


Figure 80

87/217

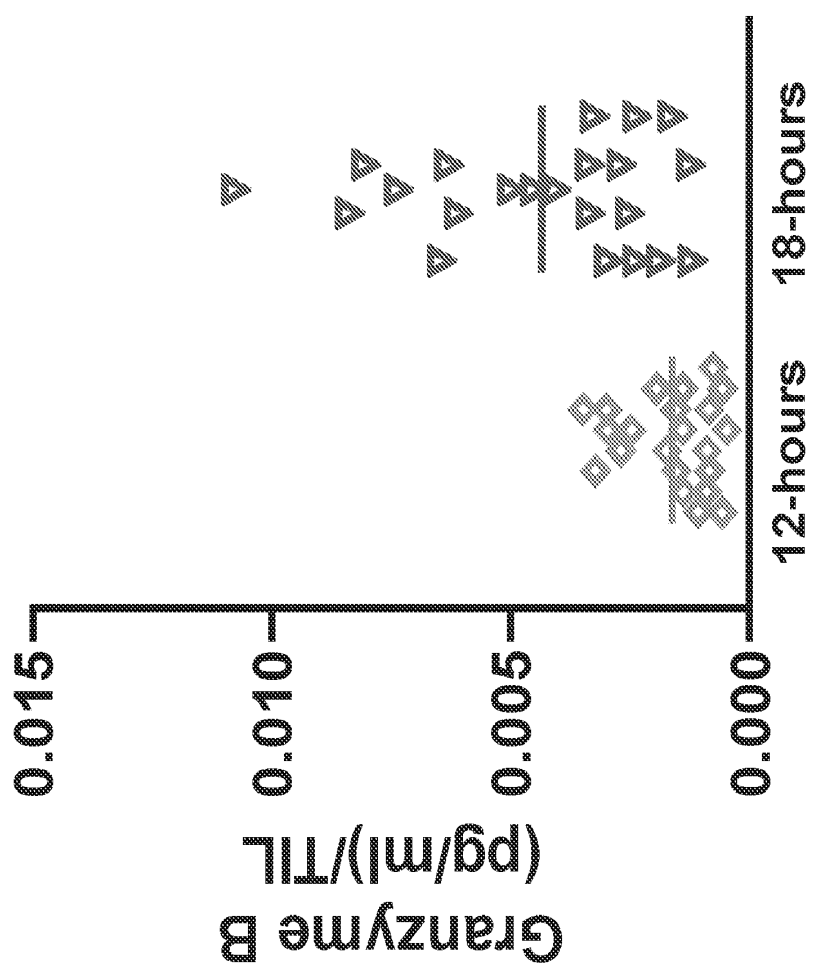


Figure 81

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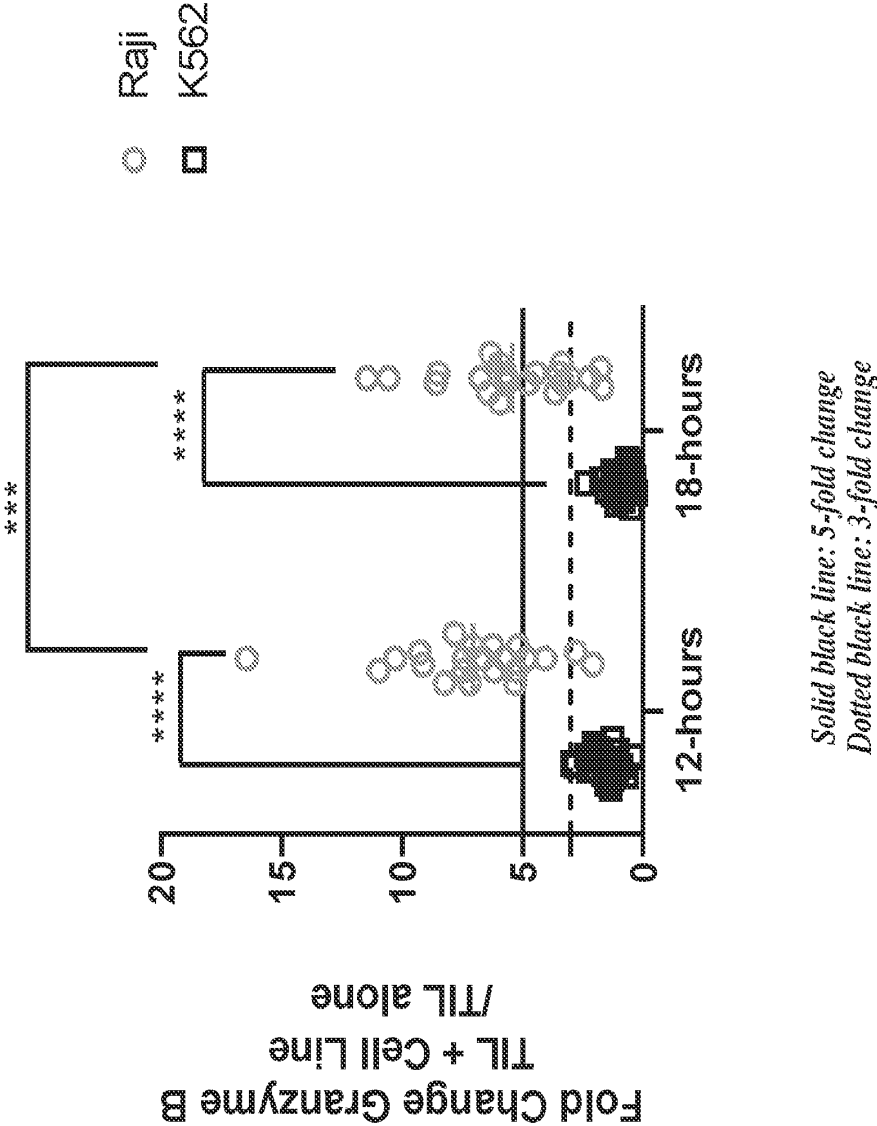


Figure 82

89/217

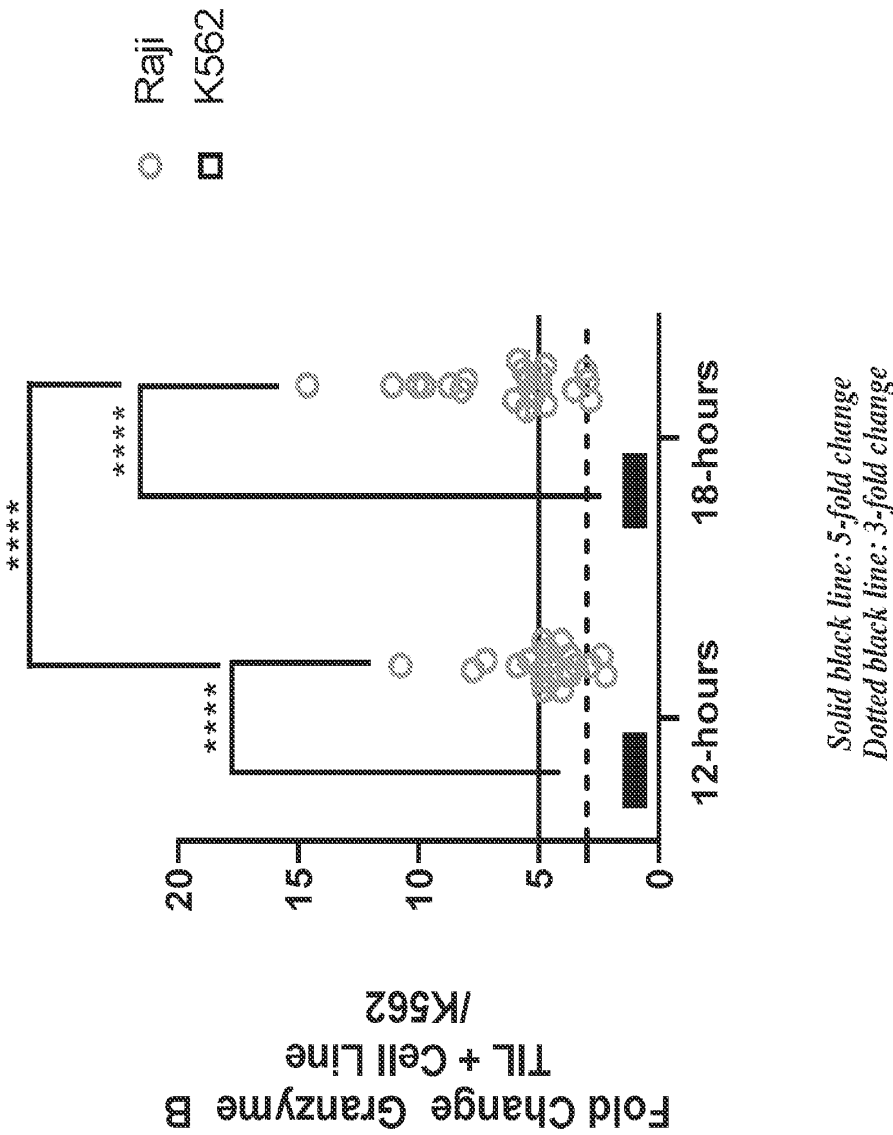
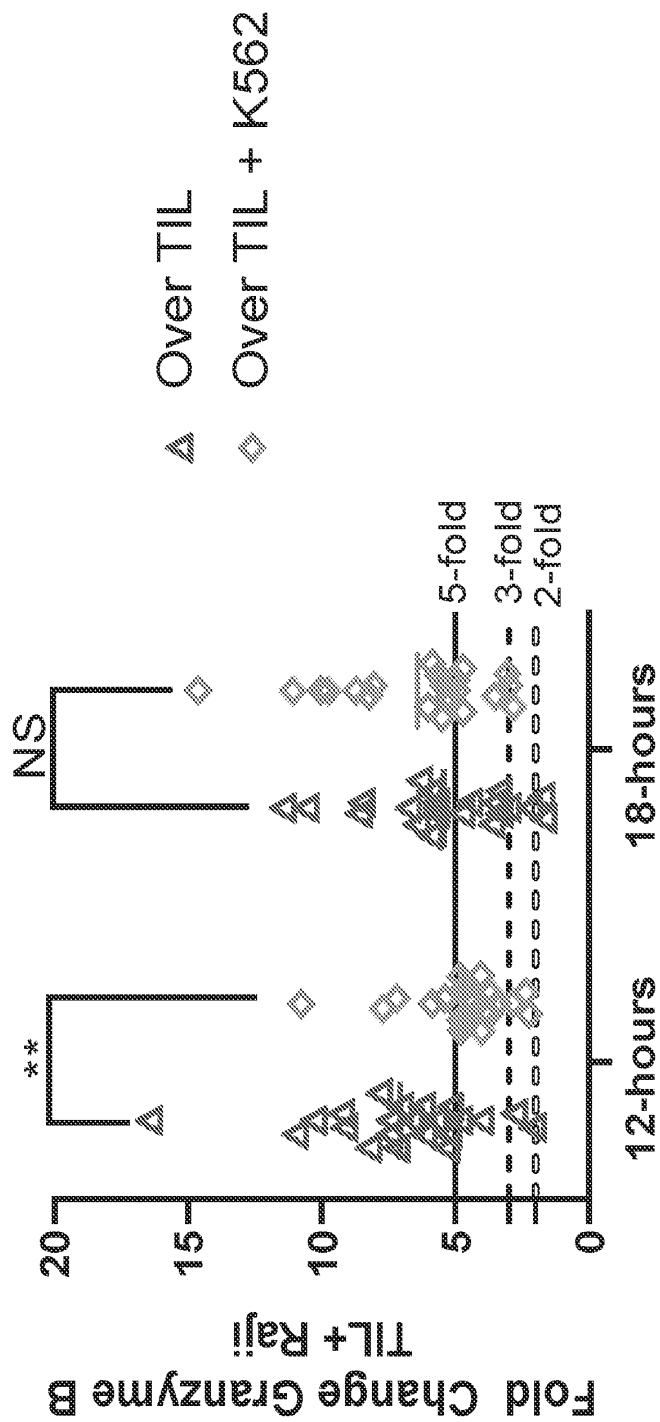


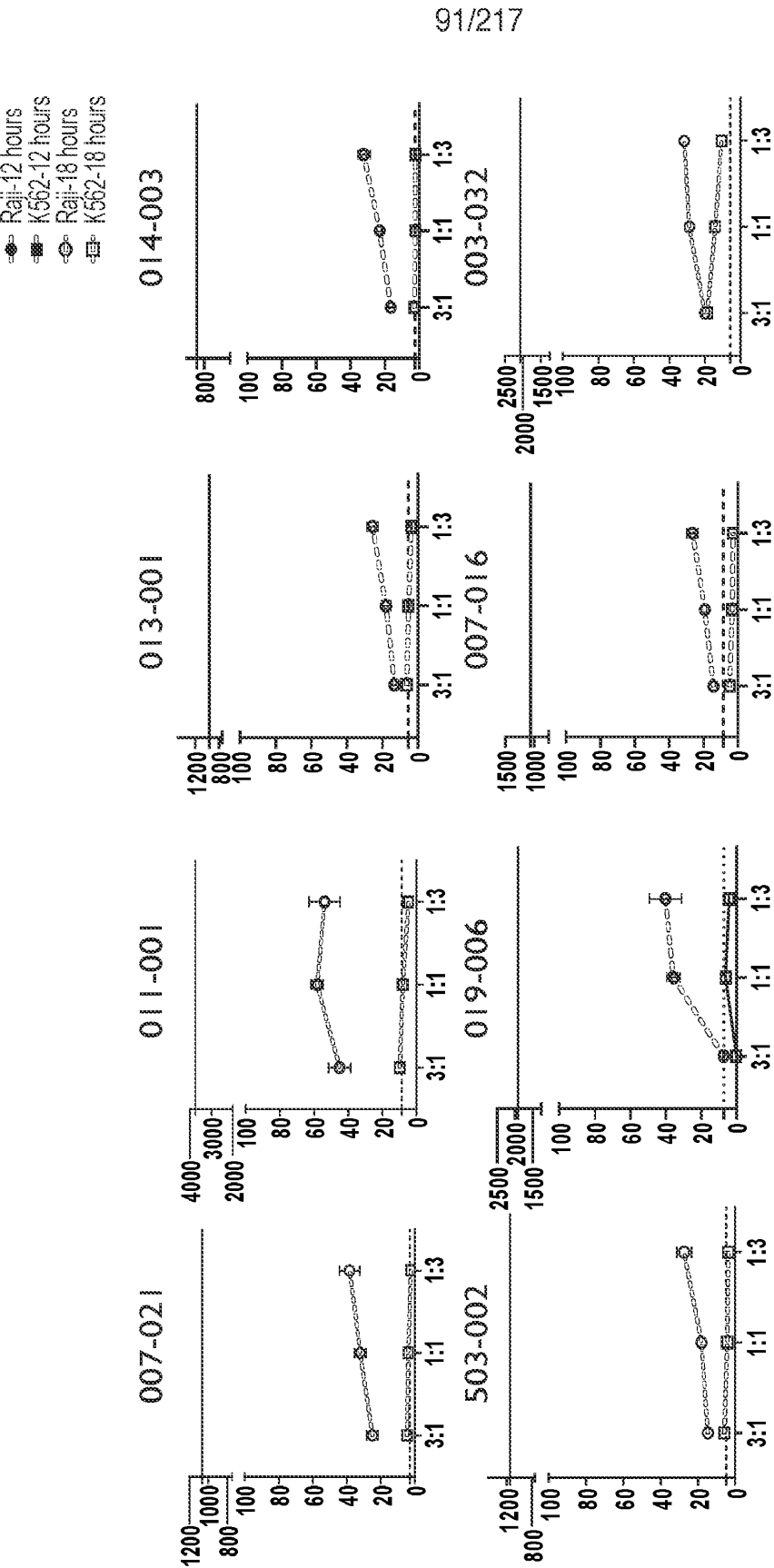
Figure 83

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Solid black line: 5-fold change
Dotted black line: 3-fold change
Dotted black and white line: 2-fold change

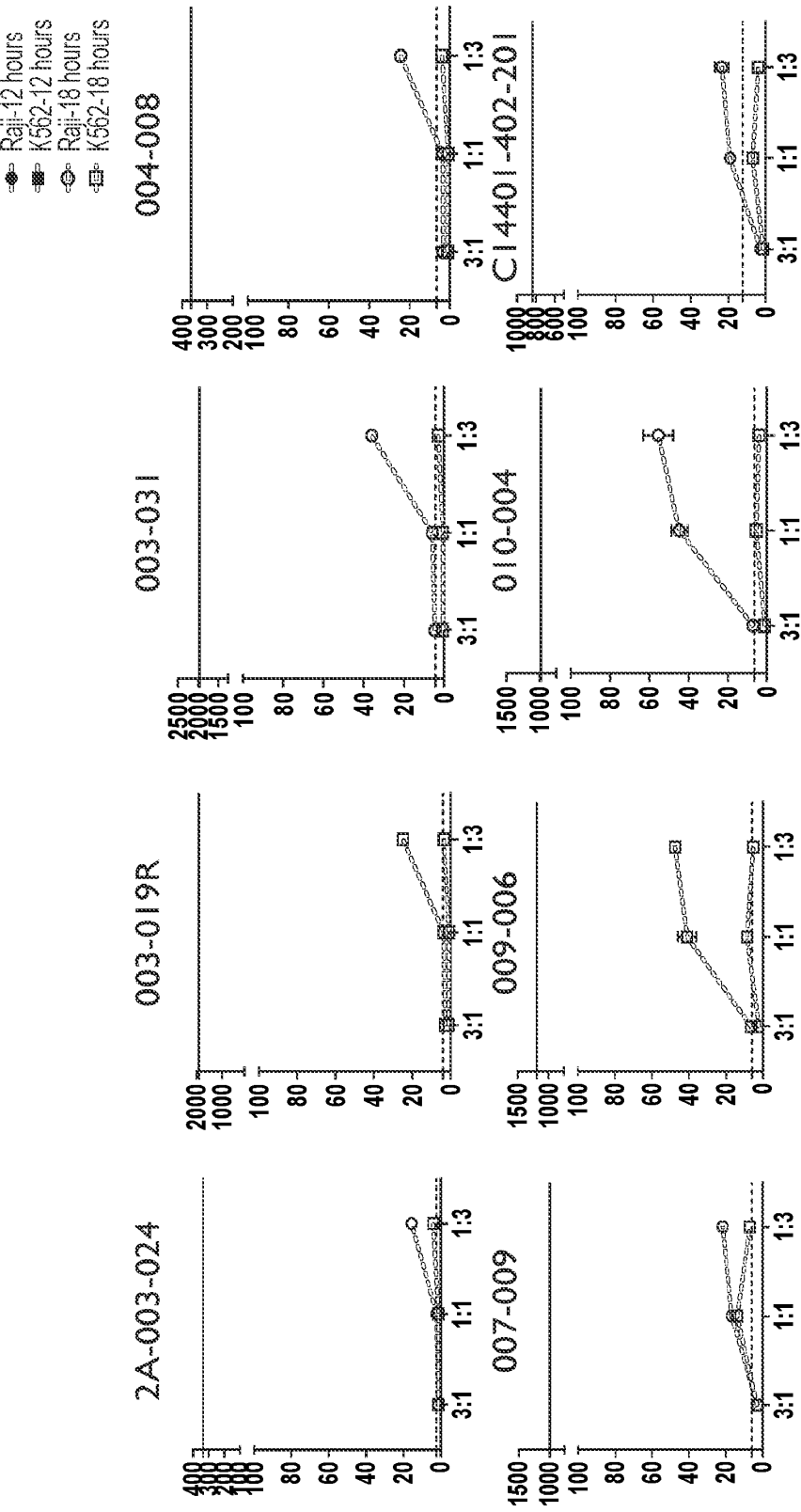
Figure 84



Solid gray line = 12 hours: α CD3/ α CD28/ α 41BB beads
Dotted gray line = 12 hours unstimulated TIL
Solid black line = 18 hours: α CD3/ α CD28/ α 41BB beads
Dotted black line = 18 hours unstimulated TIL

Figure 85

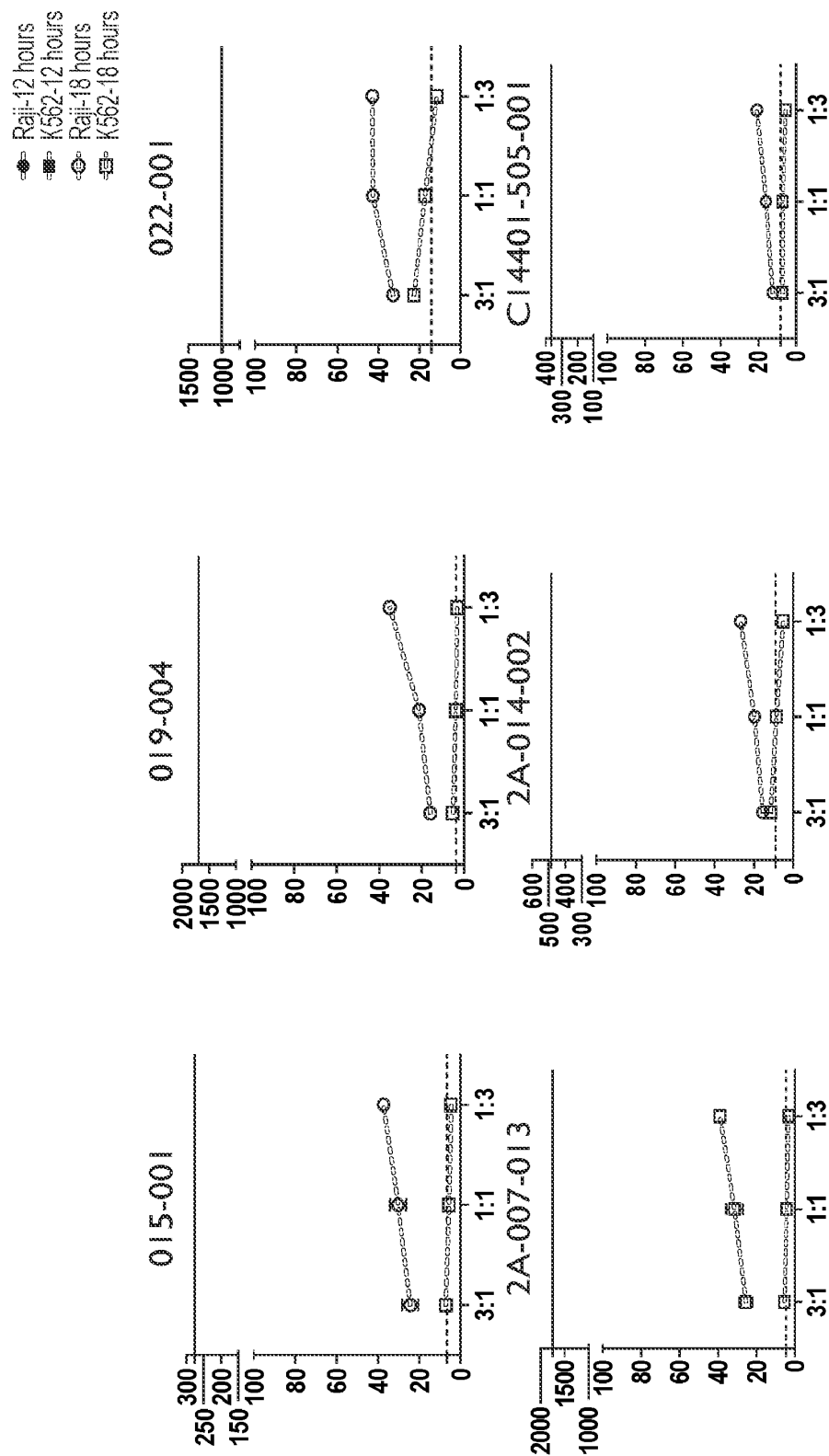
92/217



Solid gray line = 12 hours: α CD3/ α CD28/ α 41BB beads
Dotted gray line = 12 hours unstimulated TIL
Solid black line = 18 hours: α CD3/ α CD28/ α 41BB beads
Dotted black line = 18 hours unstimulated TIL

Figure 86

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Solid gray line = 12 hours; aCD3/aCD28/a41BB beads
Dotted gray line = 12 hours unstimulated TIL
Solid black line = 18 hours; aCD3/aCD28/a41BB beads
Dotted black line = 18 hours unstimulated TIL

Figure 87

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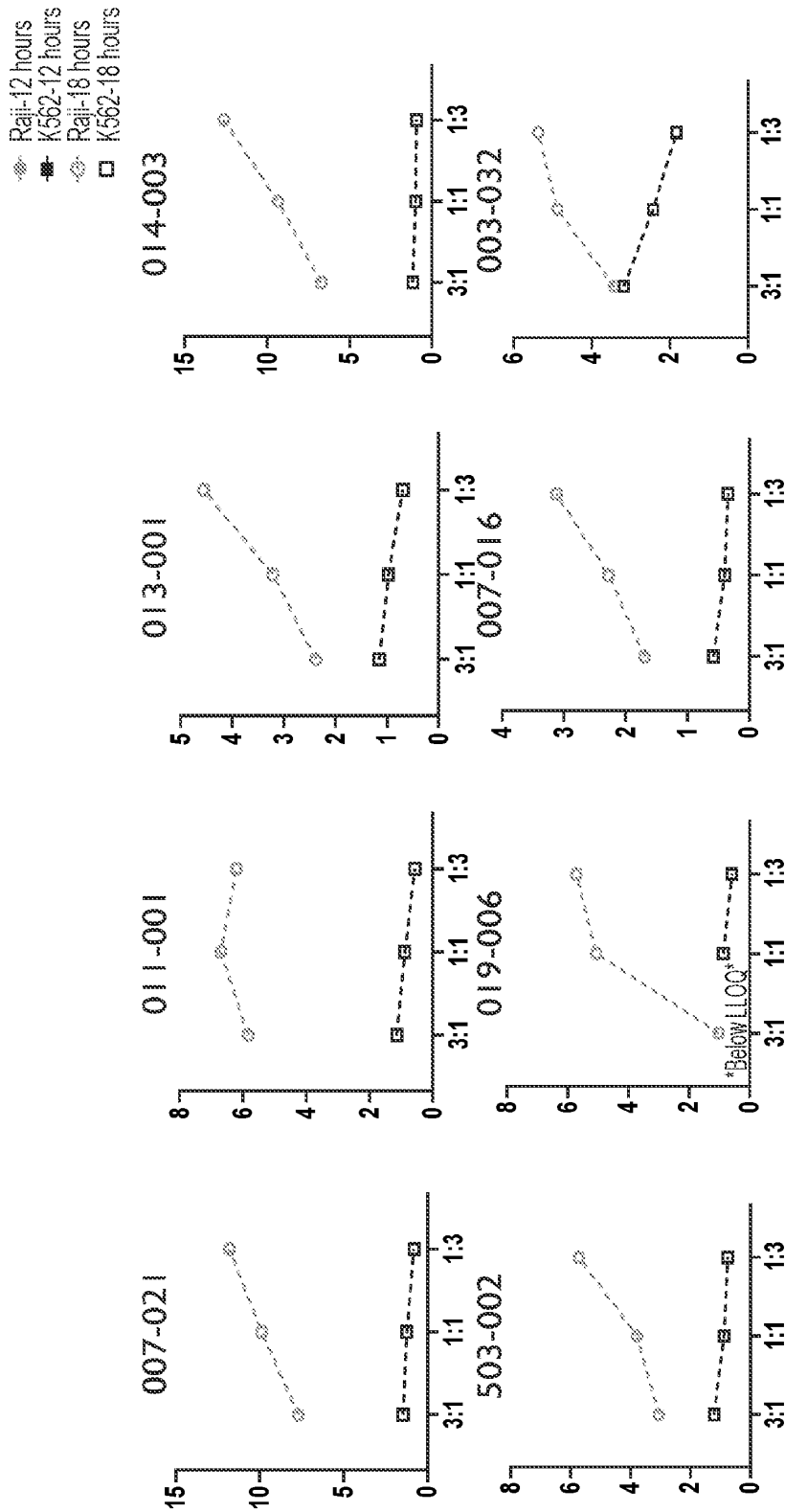


Figure 88

95/217

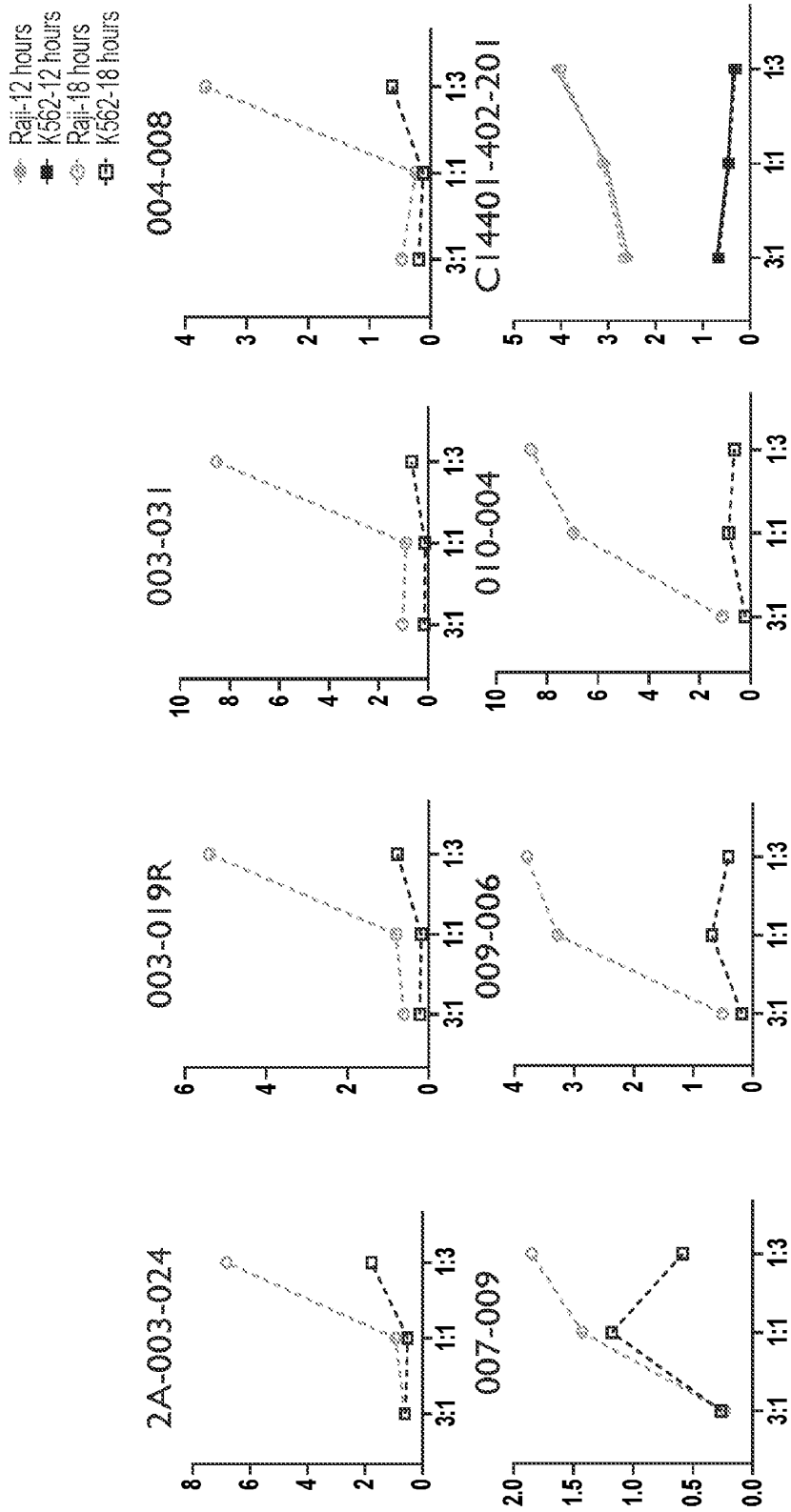


Figure 89

96/217

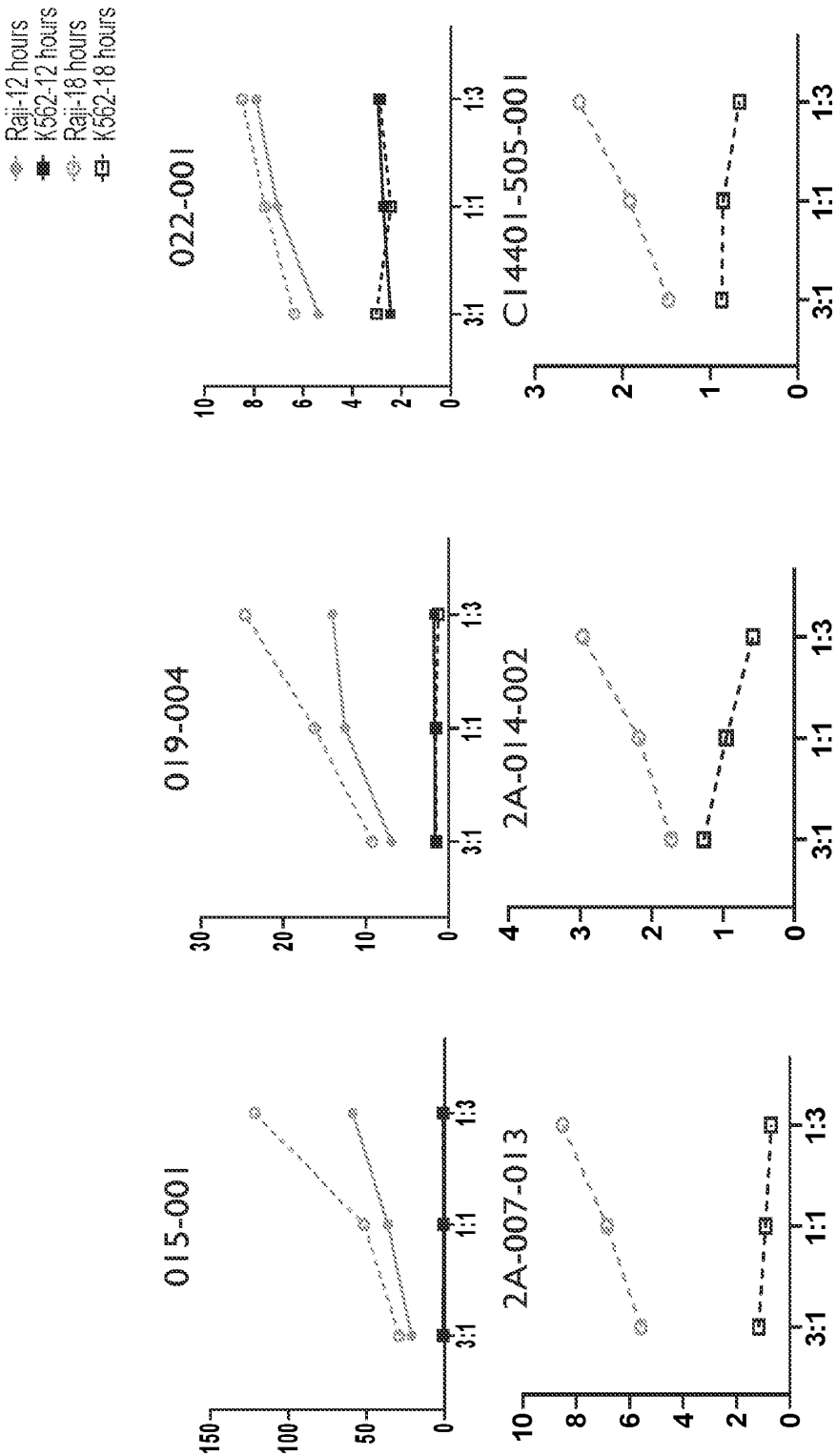


Figure 90

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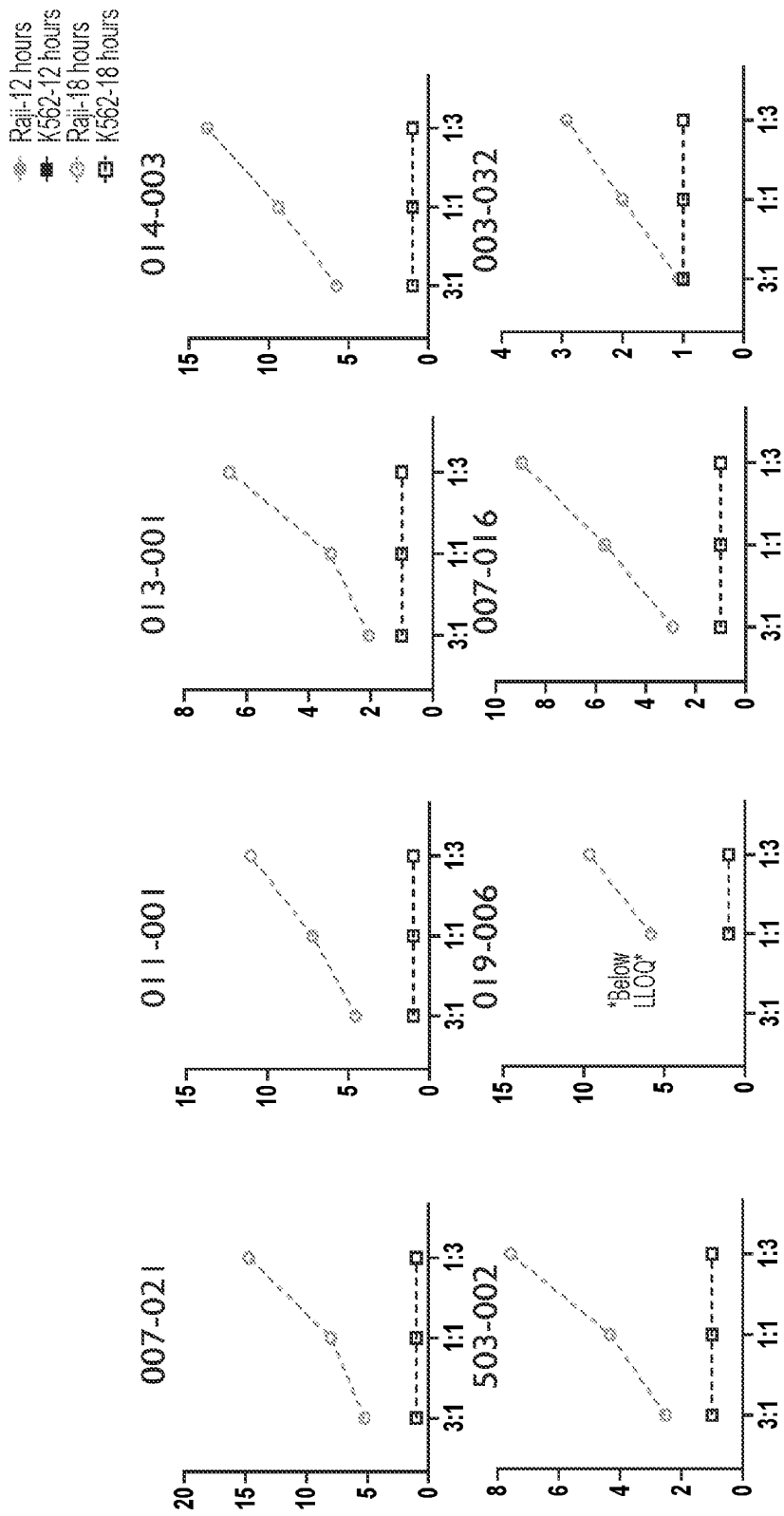


Figure 91

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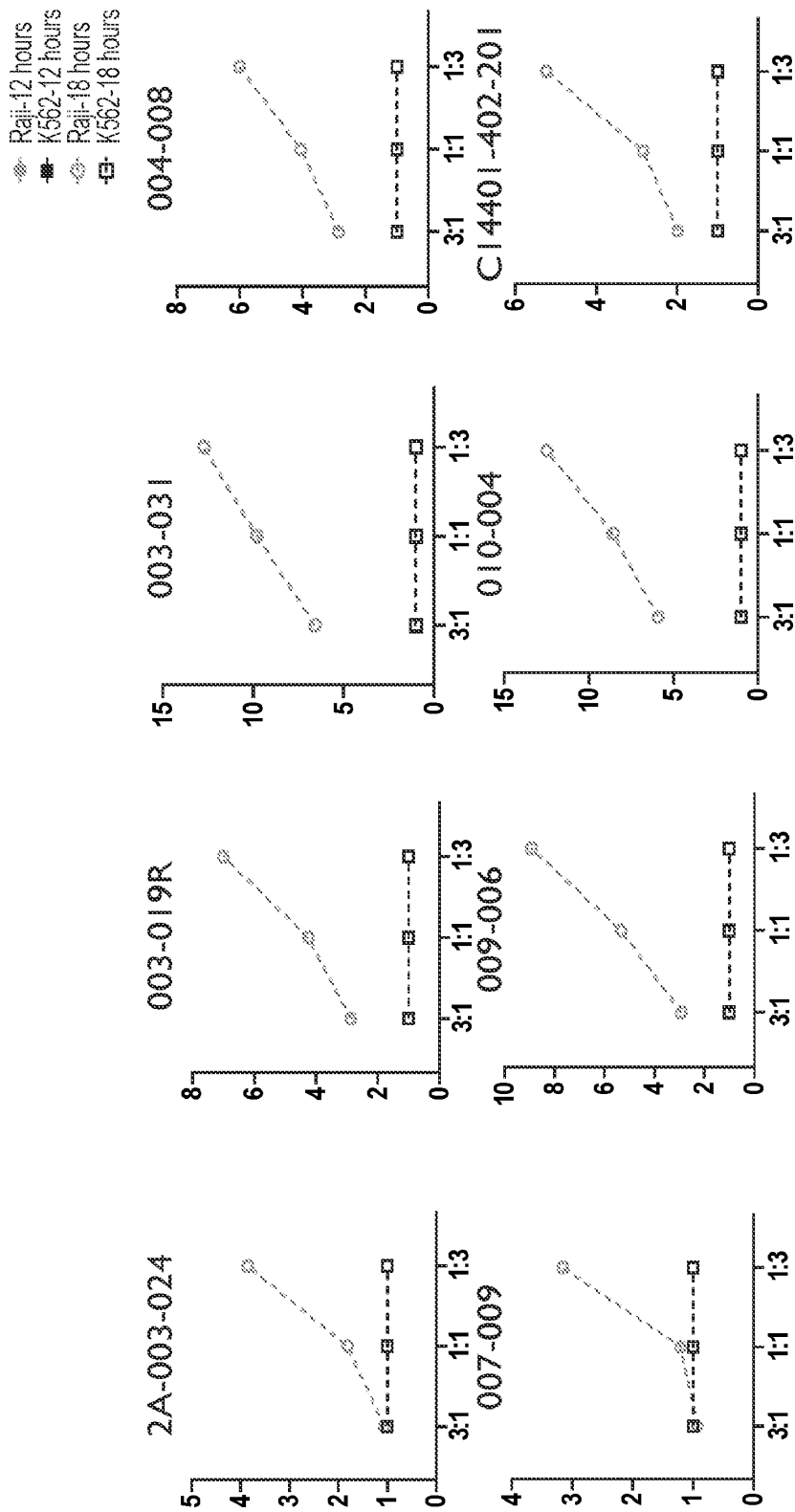


Figure 92

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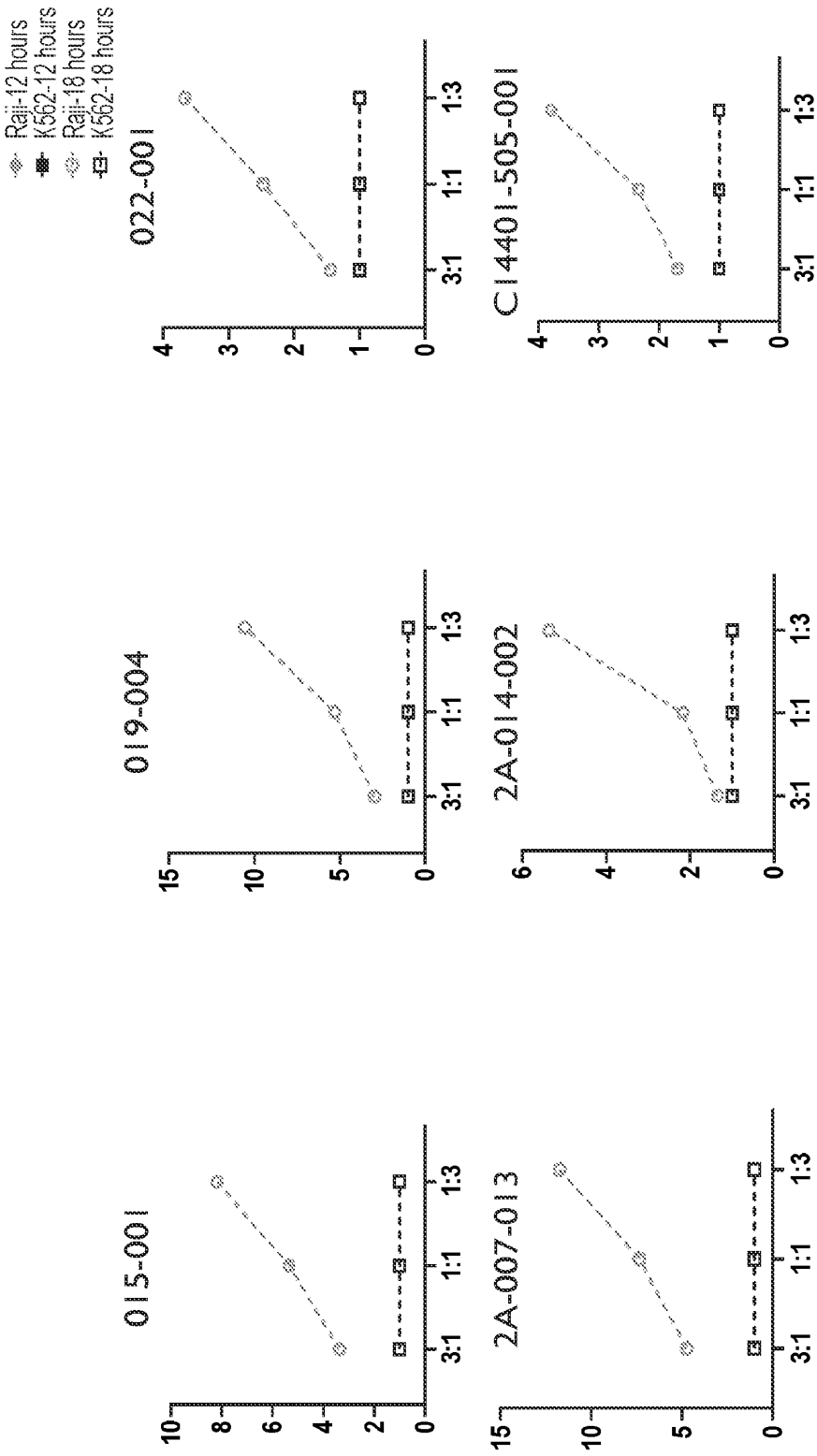


Figure 93

100/217

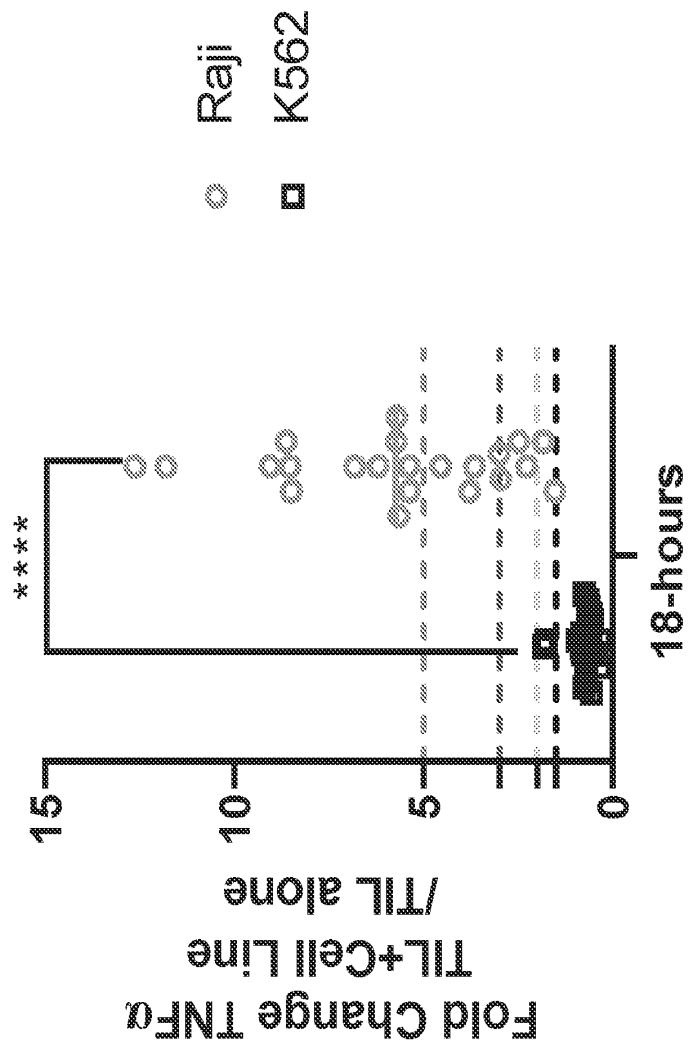


Figure 94

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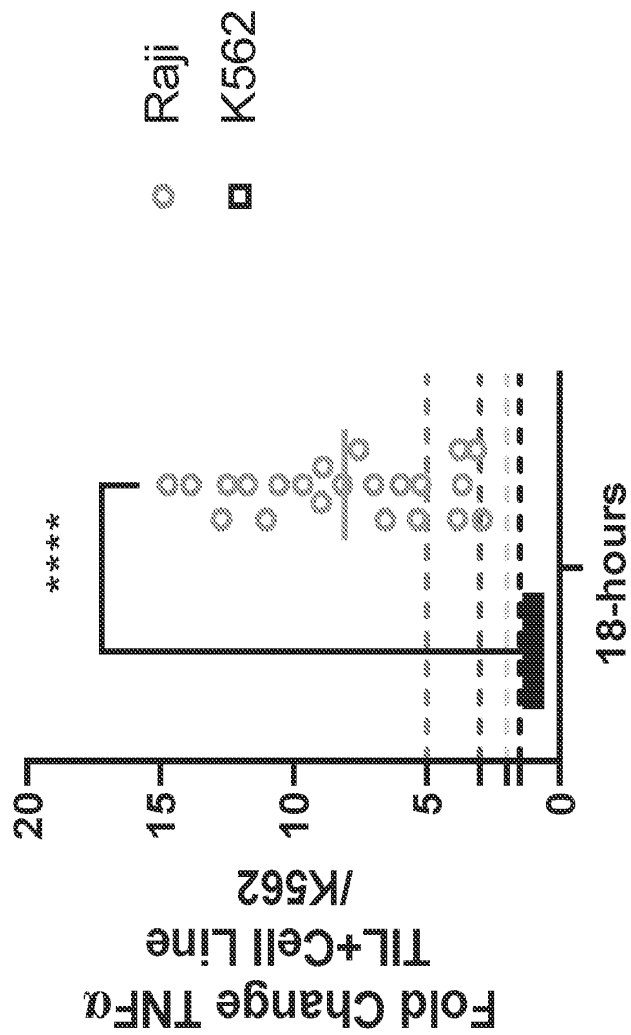


Figure 95

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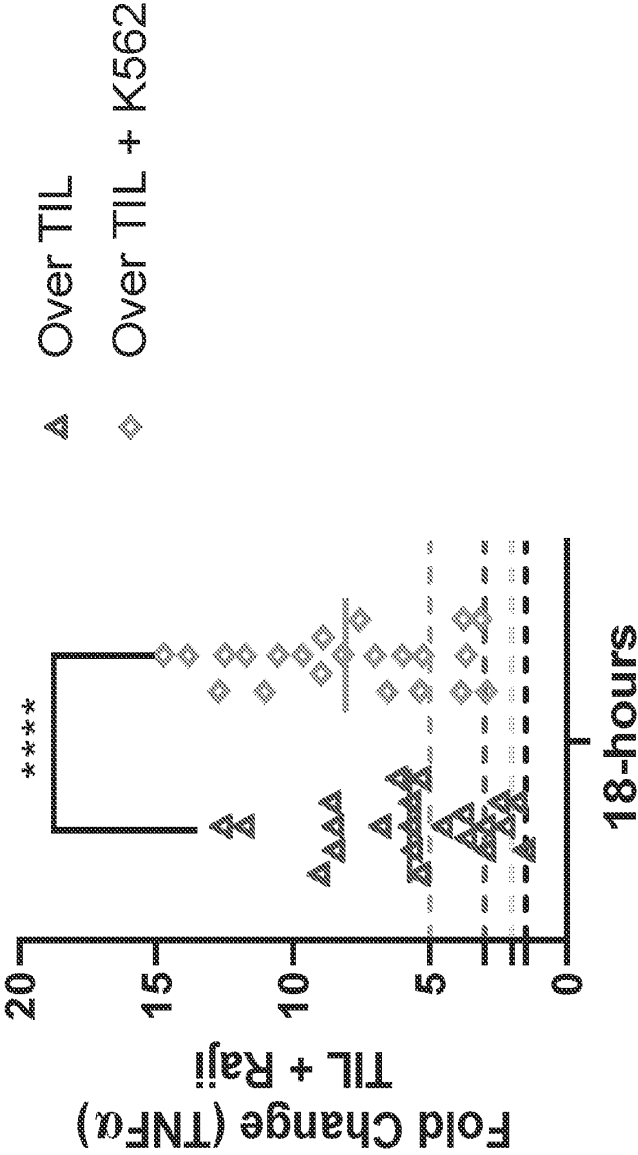


Figure 96

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Cytokine	Timepoint	Group	Mean	STDEV	Min	IQ	Median	UQ	Max	CV (%)
Granzyne B	12 hr	K562 (pg/mL)	171.8	87.3	52.7	115.7	146.0	210.7	369.7	50.8
		Raji (pg/mL)	782.5	458.5	239.0	431.0	703.0	972.7	1746.3	40.4
		K562 Fold Change over TIL	1.6	0.7	0.4	1.1	1.5	2.0	2.9	58.6
		Raji Fold Change over TIL	7.1	3.1	2.1	5.3	6.9	8.1	16.5	43.1
		K562 over K562	1	0	1	1	1	1	1	0.0
		Raji over K562	4.8	1.9	2.2	3.7	4.6	4.9	10.8	39.4
	18 hr	K562 (pg/mL)	337.8	175.8	119.0	217.0	311.5	378.0	853.0	52.0
		Raji (pg/mL)	2105.1	1297.4	603.3	1185.3	1672.7	3051.3	5383.7	54.6
		K562 Fold Change over TIL	0.9	0.5	0.3	0.5	0.9	1.2	2.3	61.6
		Raji Fold Change over TIL	5.4	2.6	1.7	3.4	5.7	6.4	11.5	48.6
		K562 over K562	1	0	1	1	1	1	1	0.0
		Raji over K562	6.4	3.0	2.8	4.8	5.5	8.2	14.6	46.2
IFN- γ	12 hr	K562 (pg/mL)	16.0	18.4	1.8	6.3	10.5	16.2	69.1	114.8
		Raji (pg/mL)	198.4	245.3	19.5	50.7	106.5	196.0	1022.7	194.1
		K562 Fold Change over TIL	3.0	5.8	0.4	0.9	1.2	1.7	26.3	123.7
		Raji Fold Change over TIL	26.7	26.2	2.0	7.9	14.1	46.2	92.9	97.8
		K562 over K562	1	0	1	1	1	1	1	0.0
		Raji over K562	20.3	22.9	1.0	5.0	12.9	25.1	83.7	112.5
	18 hr	K562 (pg/mL)	17.7	20.0	1.9	7.4	12.7	17.4	77.9	113.2
		Raji (pg/mL)	379.8	526.0	26.6	99.9	164.0	430.7	2112.7	194.0
		K562 Fold Change over TIL	3.1	6.0	0.3	0.9	1.0	2.0	27.1	138.5
		Raji Fold Change over TIL	45.3	49.1	2.8	12.3	23.0	73.4	154.7	108.3
		K562 over K562	1	0	1	1	1	1	1	0.0
		Raji over K562	36.8	47.7	1.5	6.2	14.4	44.1	157.5	129.7

Figure 97

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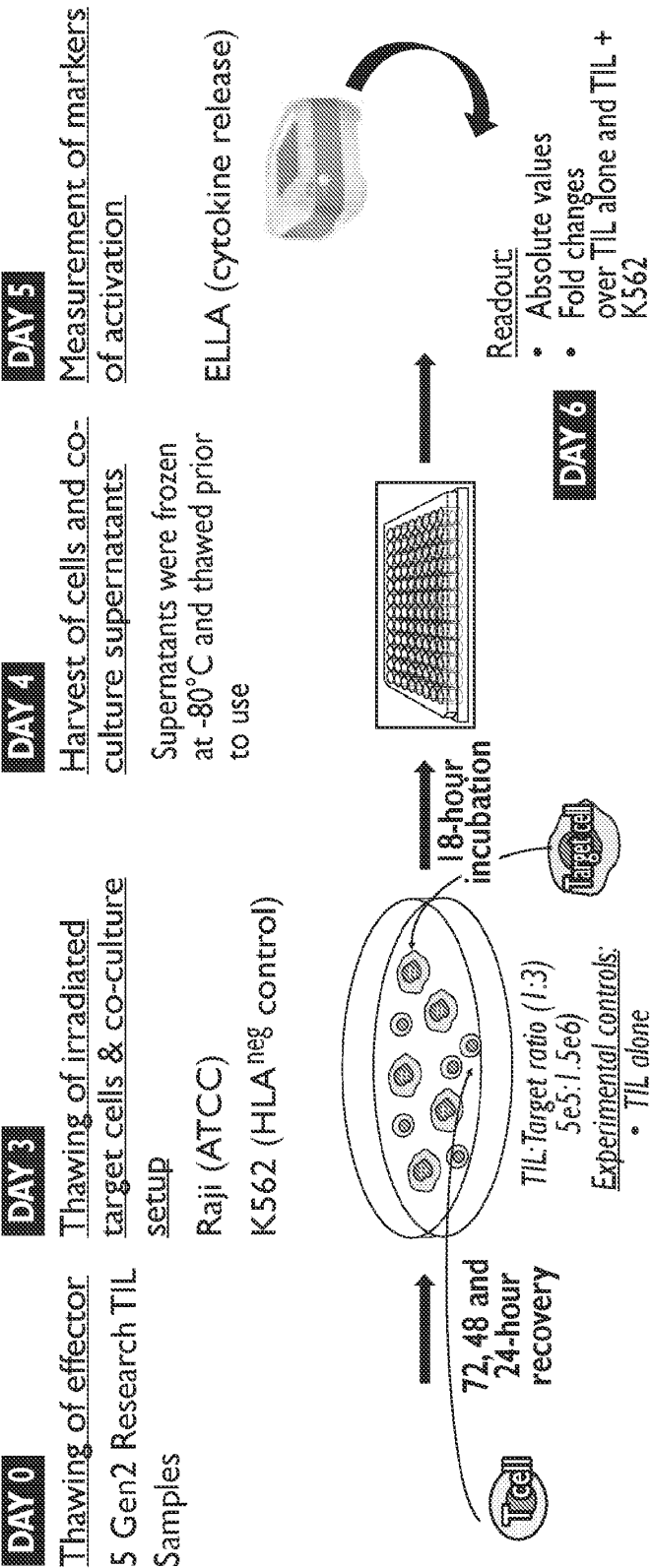


Figure 98

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- ▲ 72-hour
- ◆ 48-hour
- 24-hour

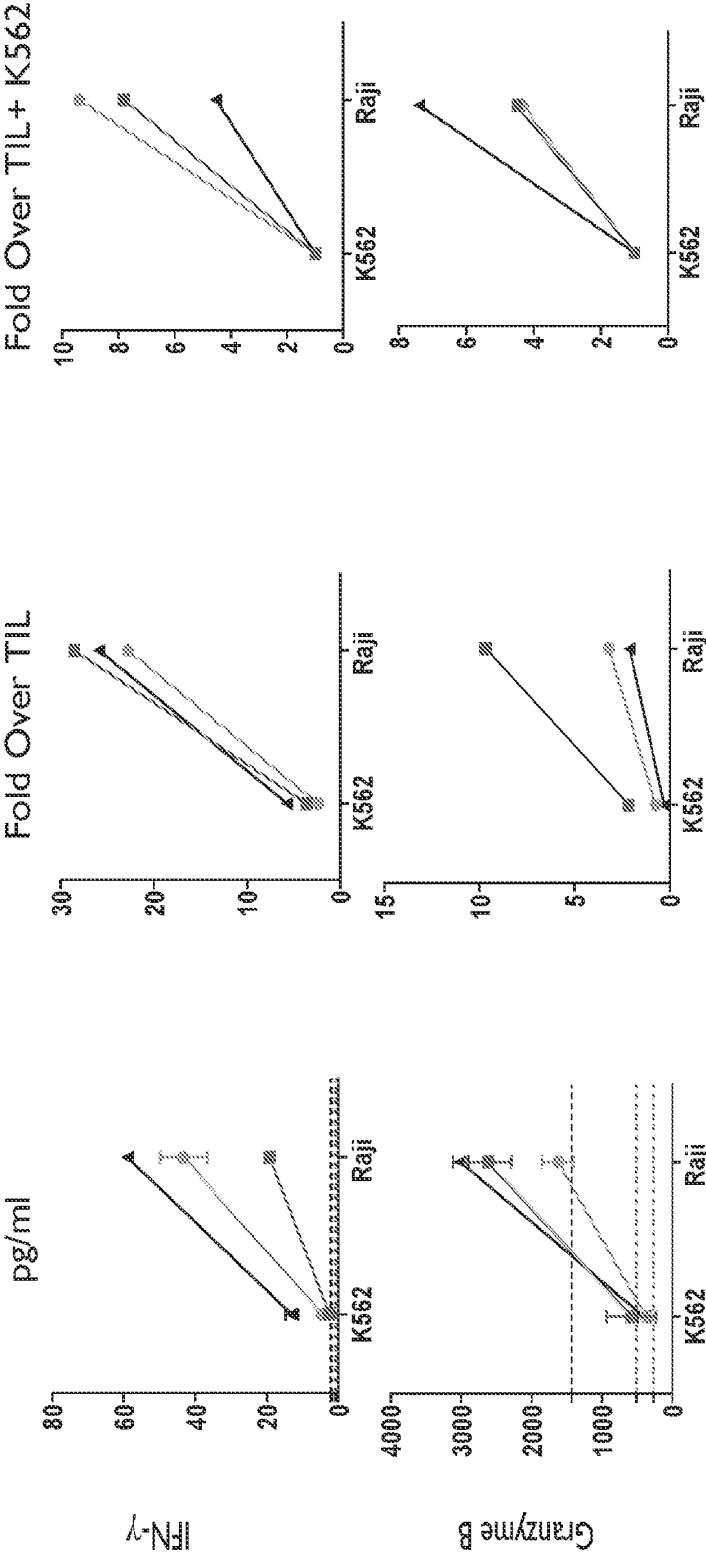


Figure 99

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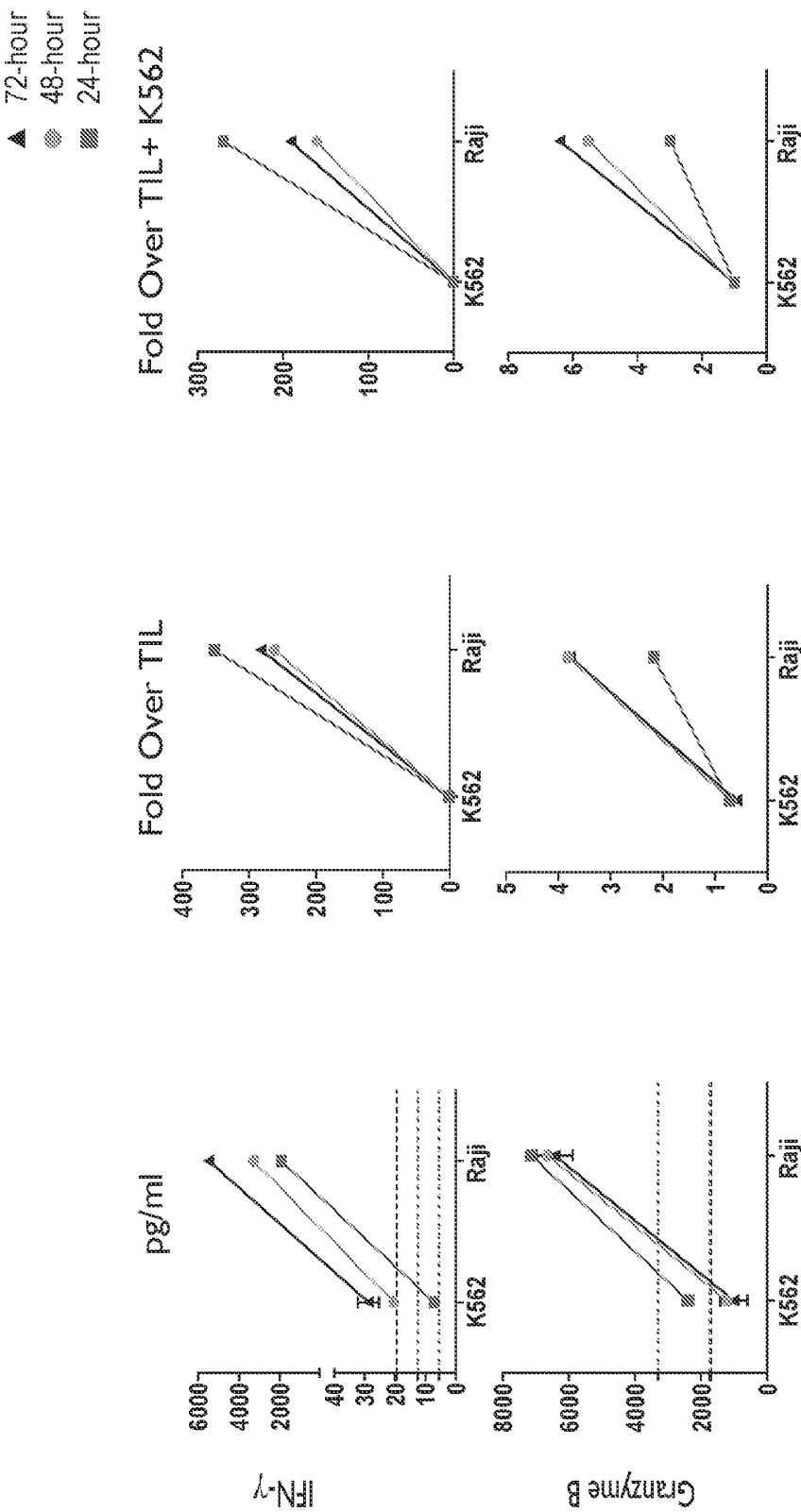


Figure 100

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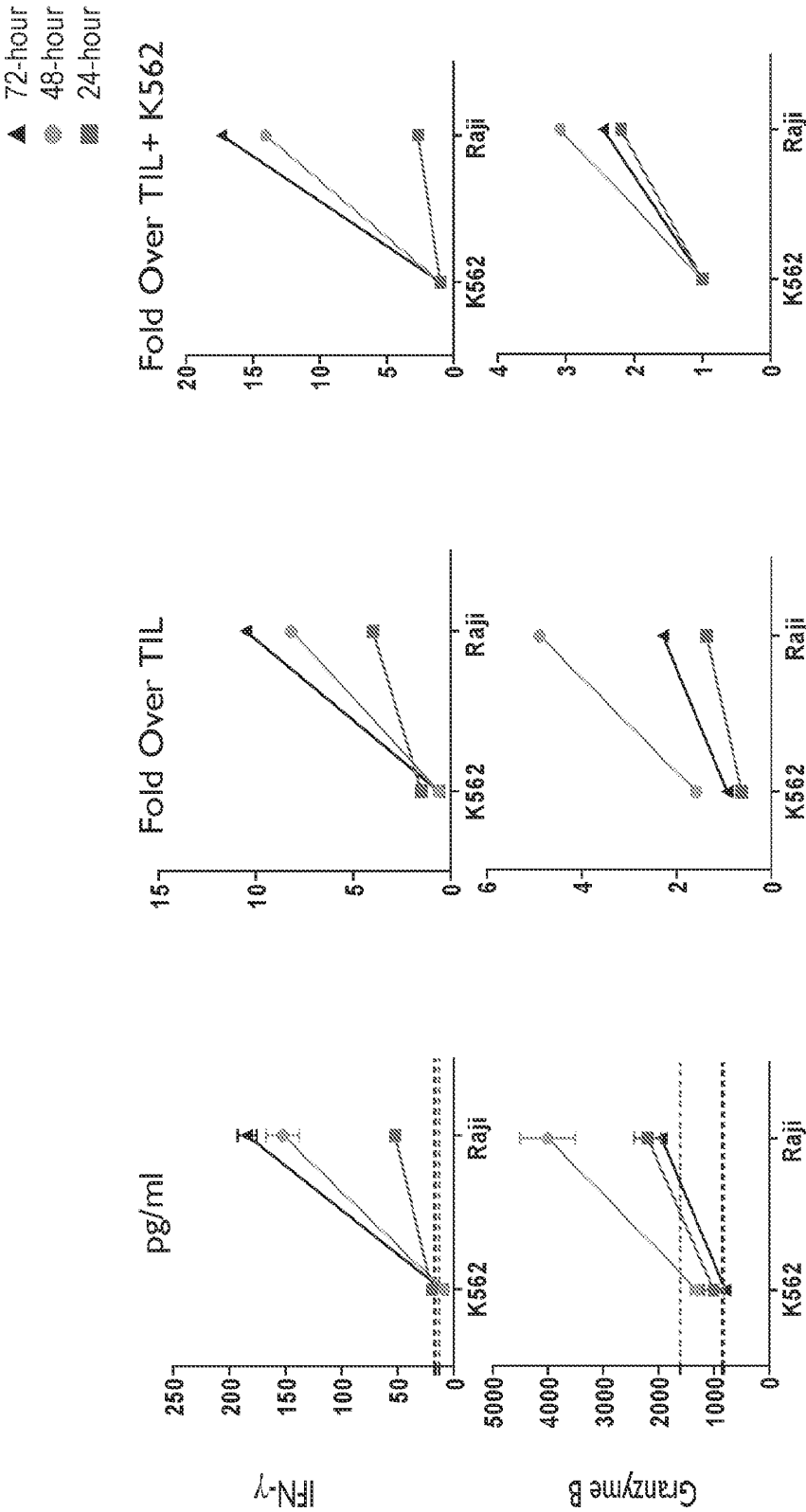


Figure 101

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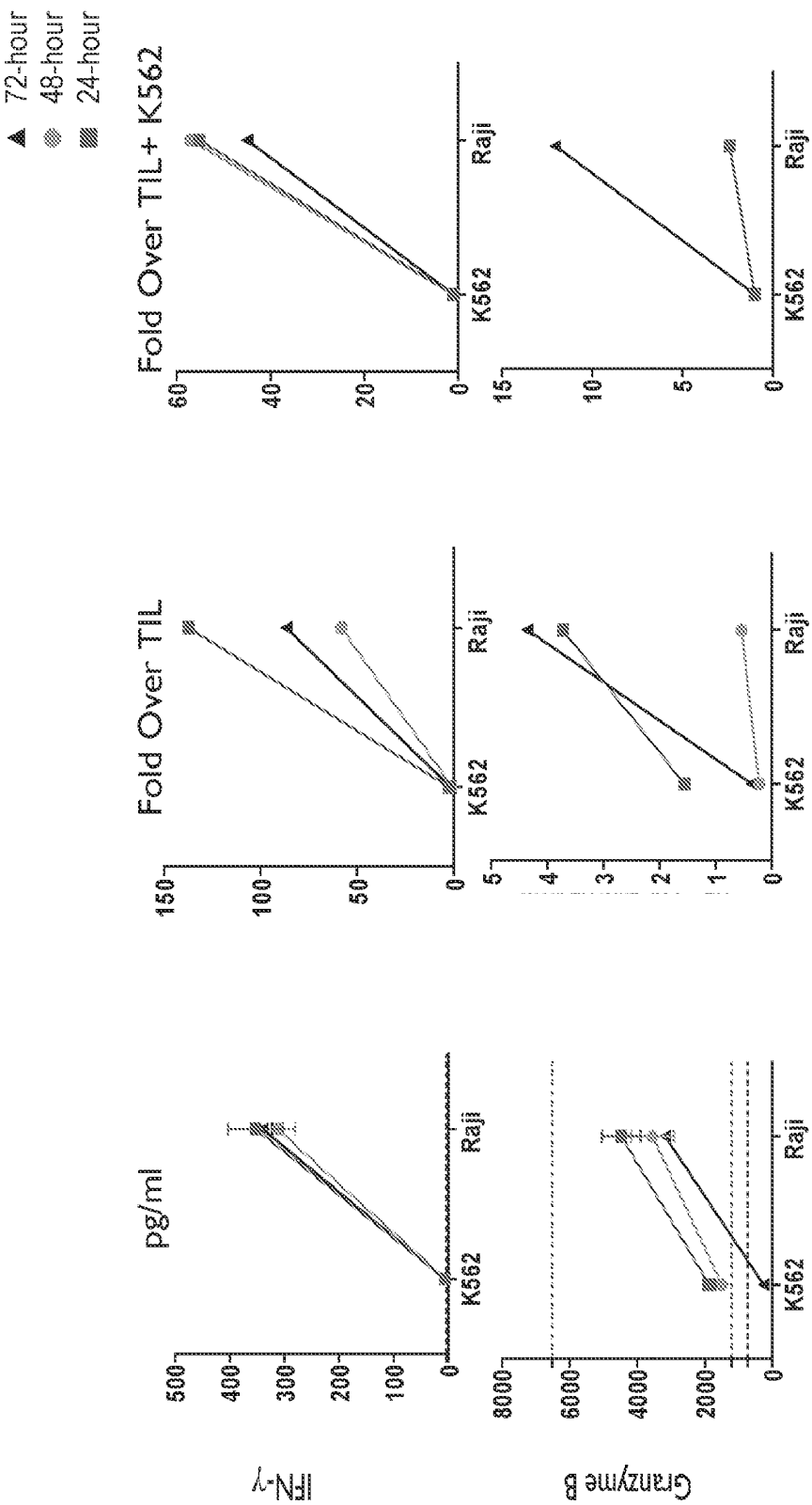


Figure 102

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- ▲ 72-hour
- ◆ 48-hour
- ▨ 24-hour

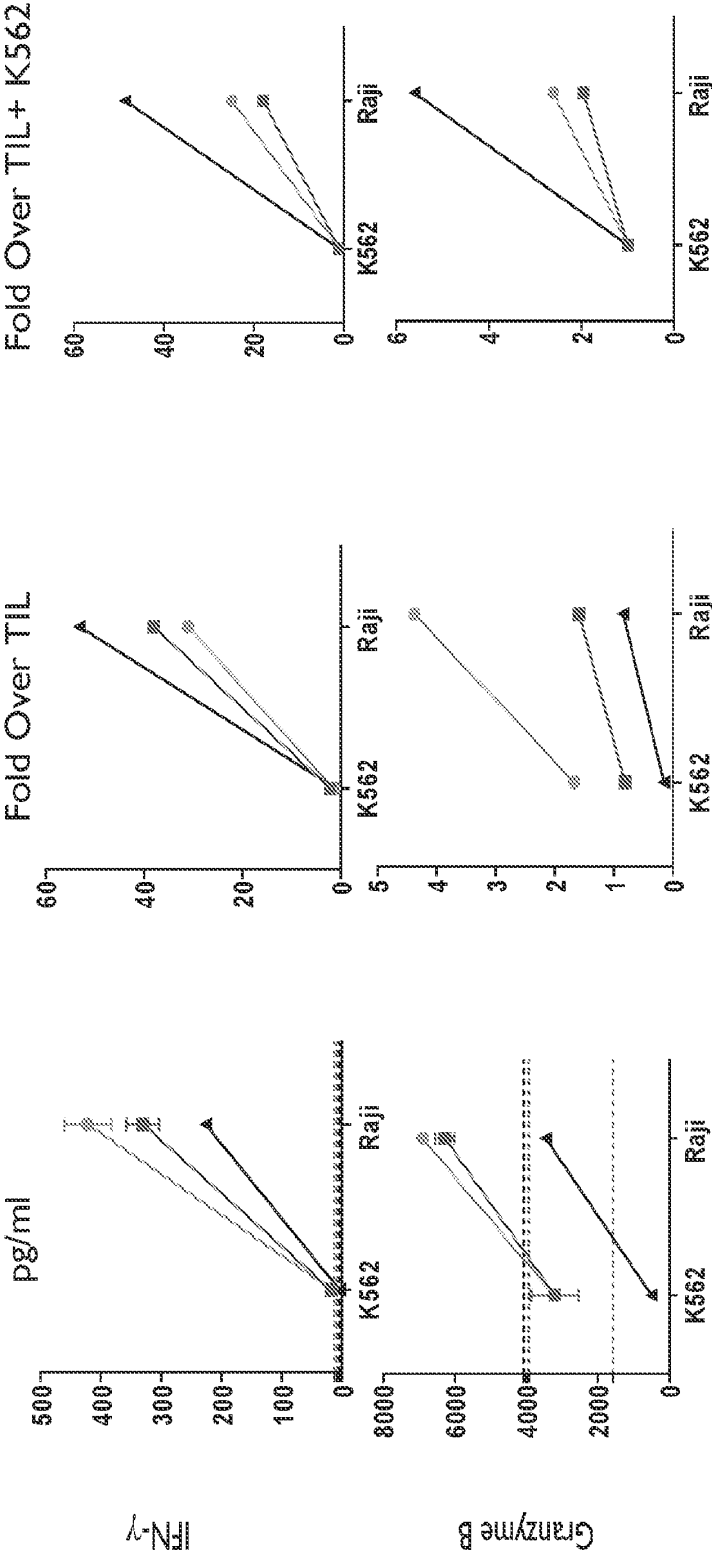


Figure 103

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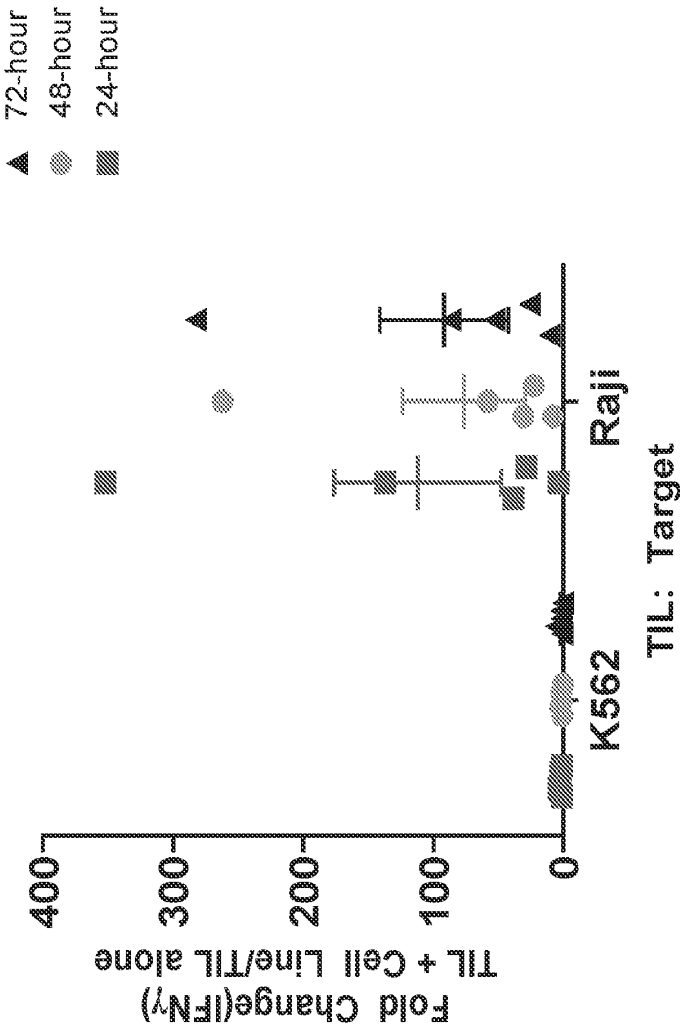


Figure 104

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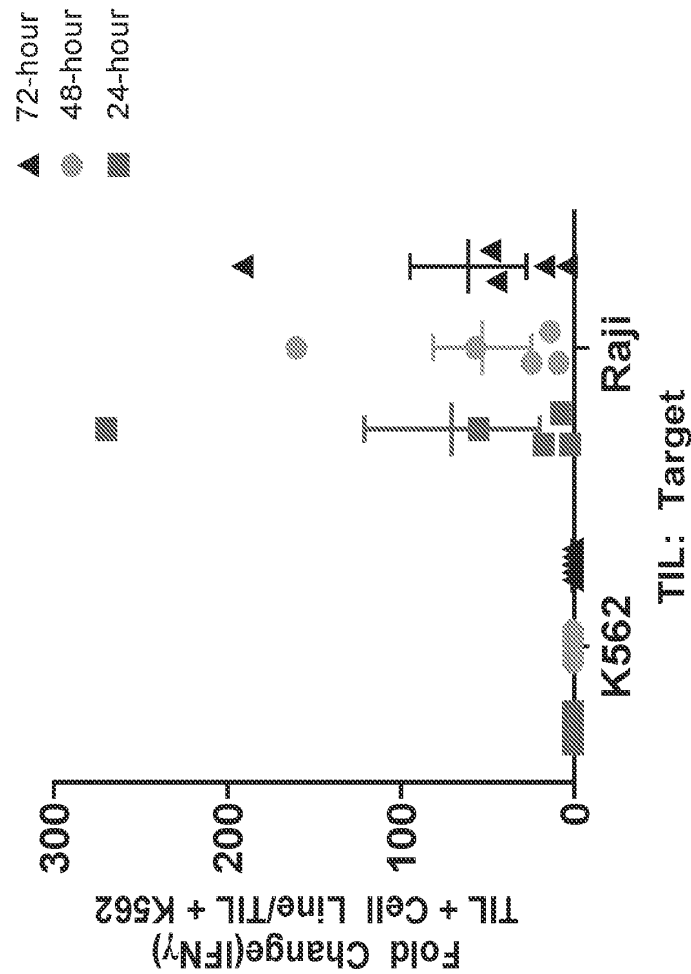


Figure 105

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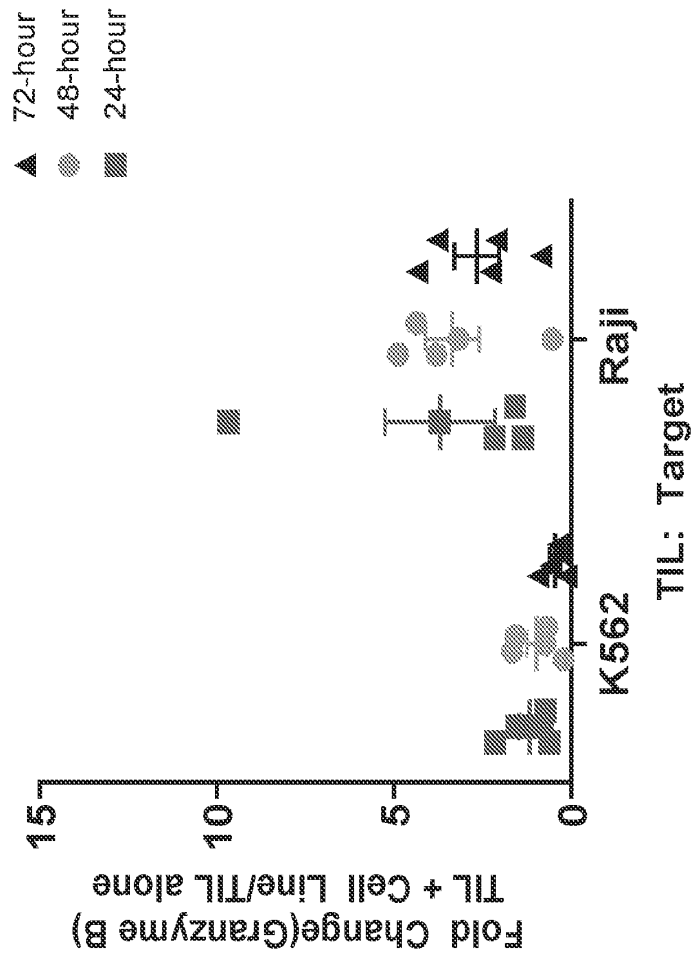


Figure 106

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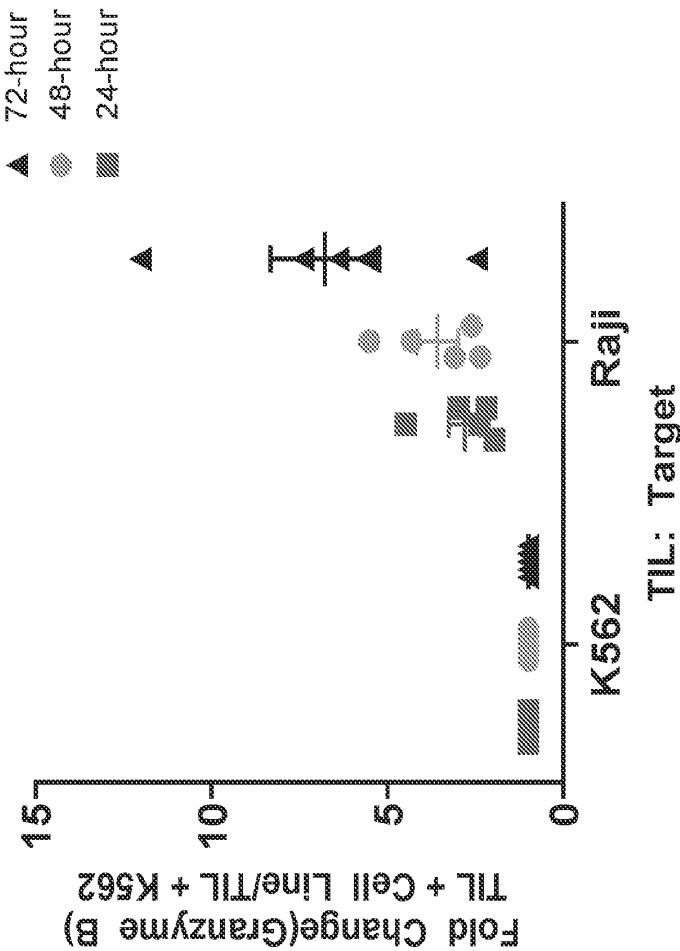


Figure 107

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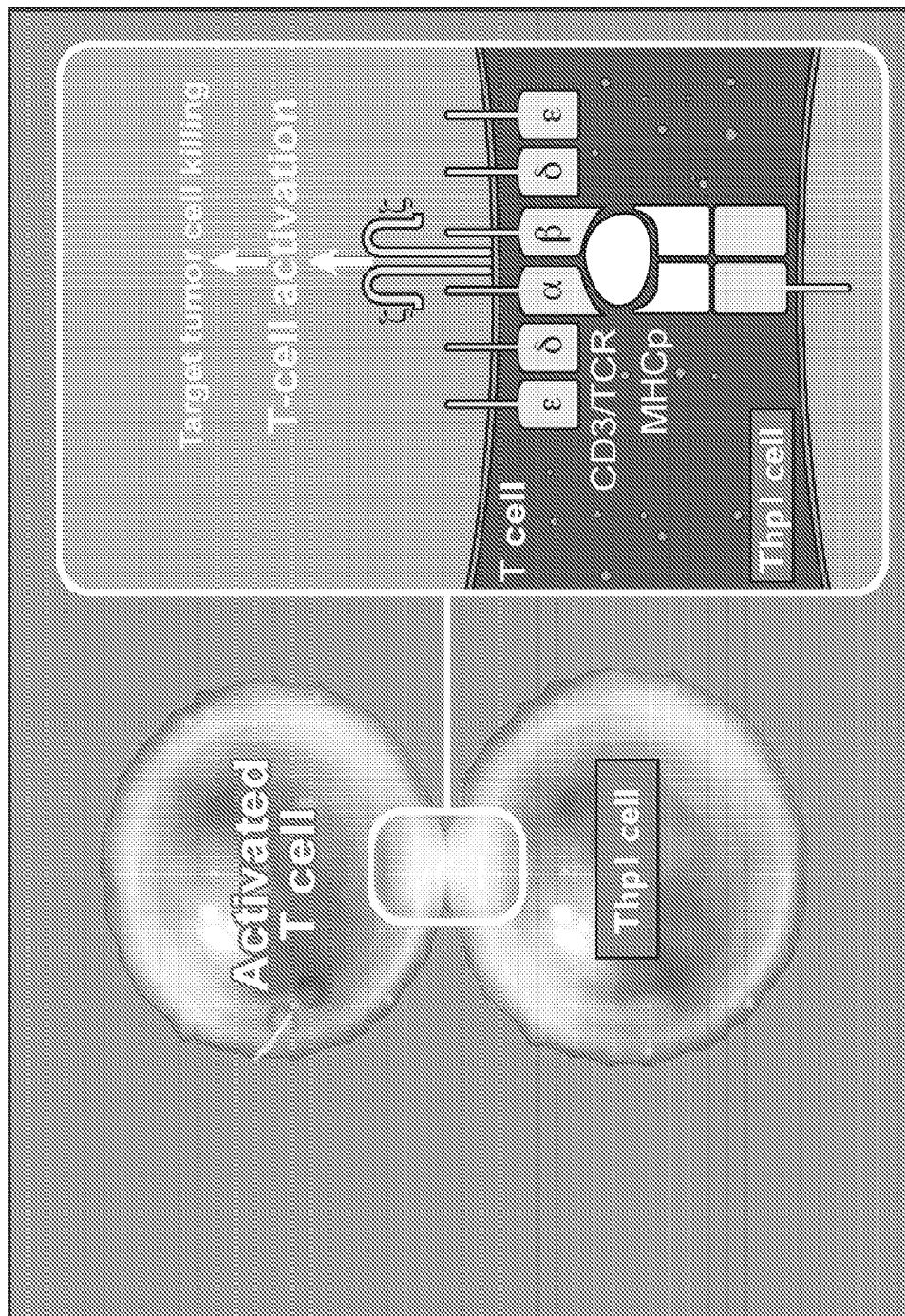


Figure 108

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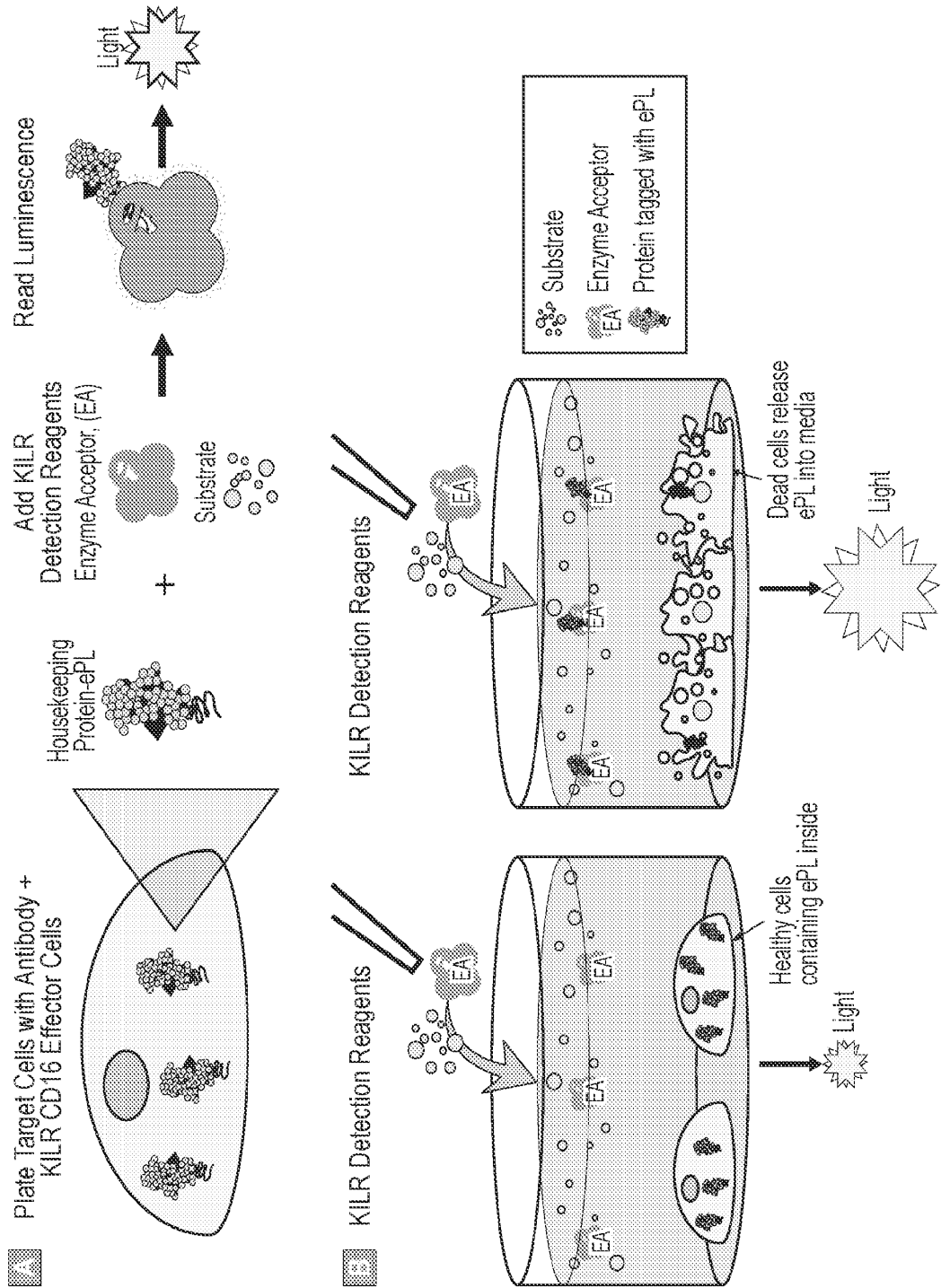


Figure 109

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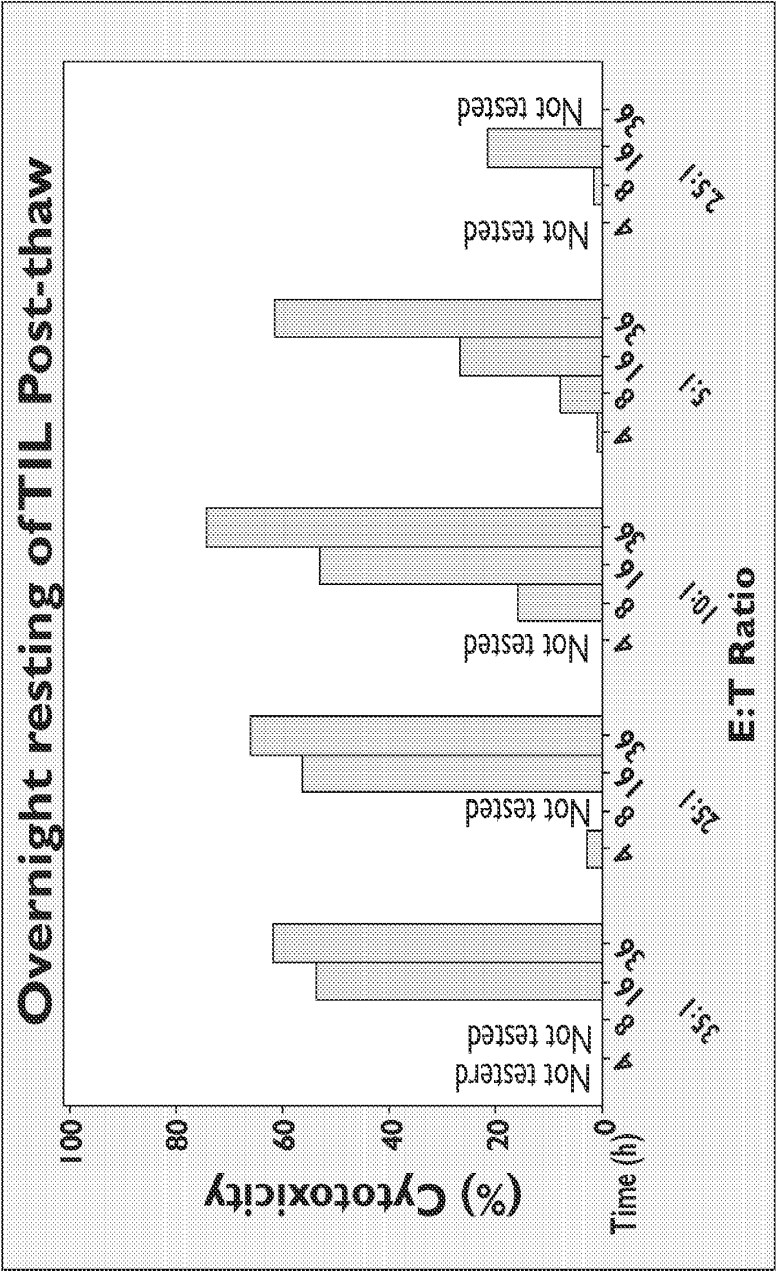


Figure 110

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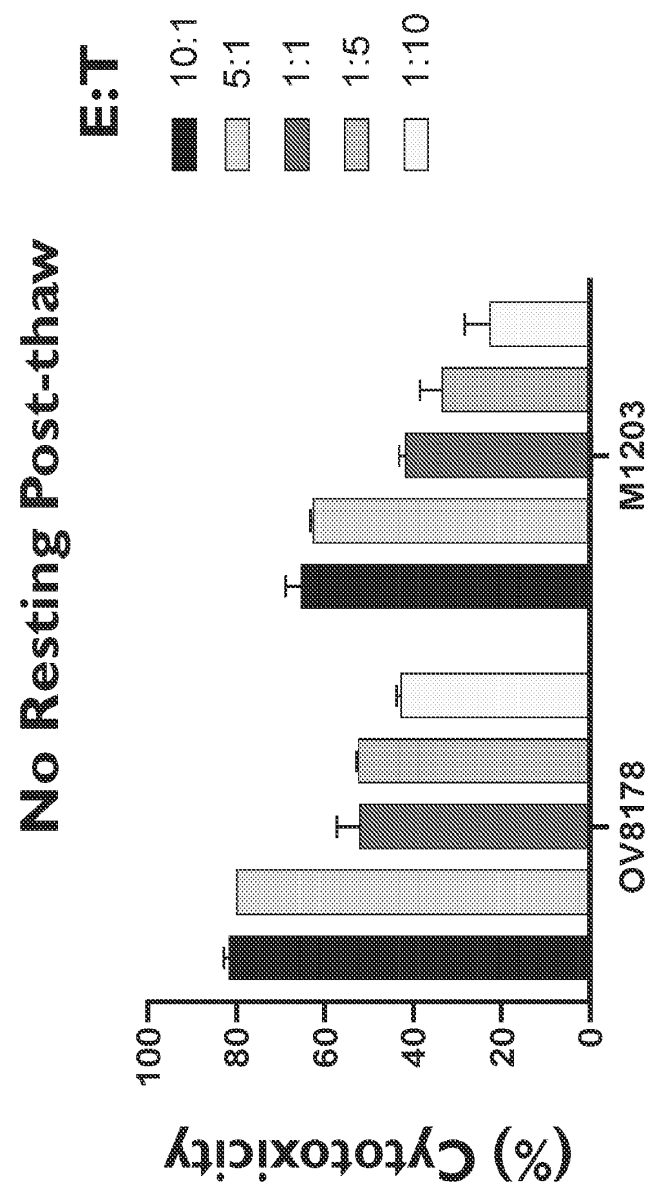


Figure 111

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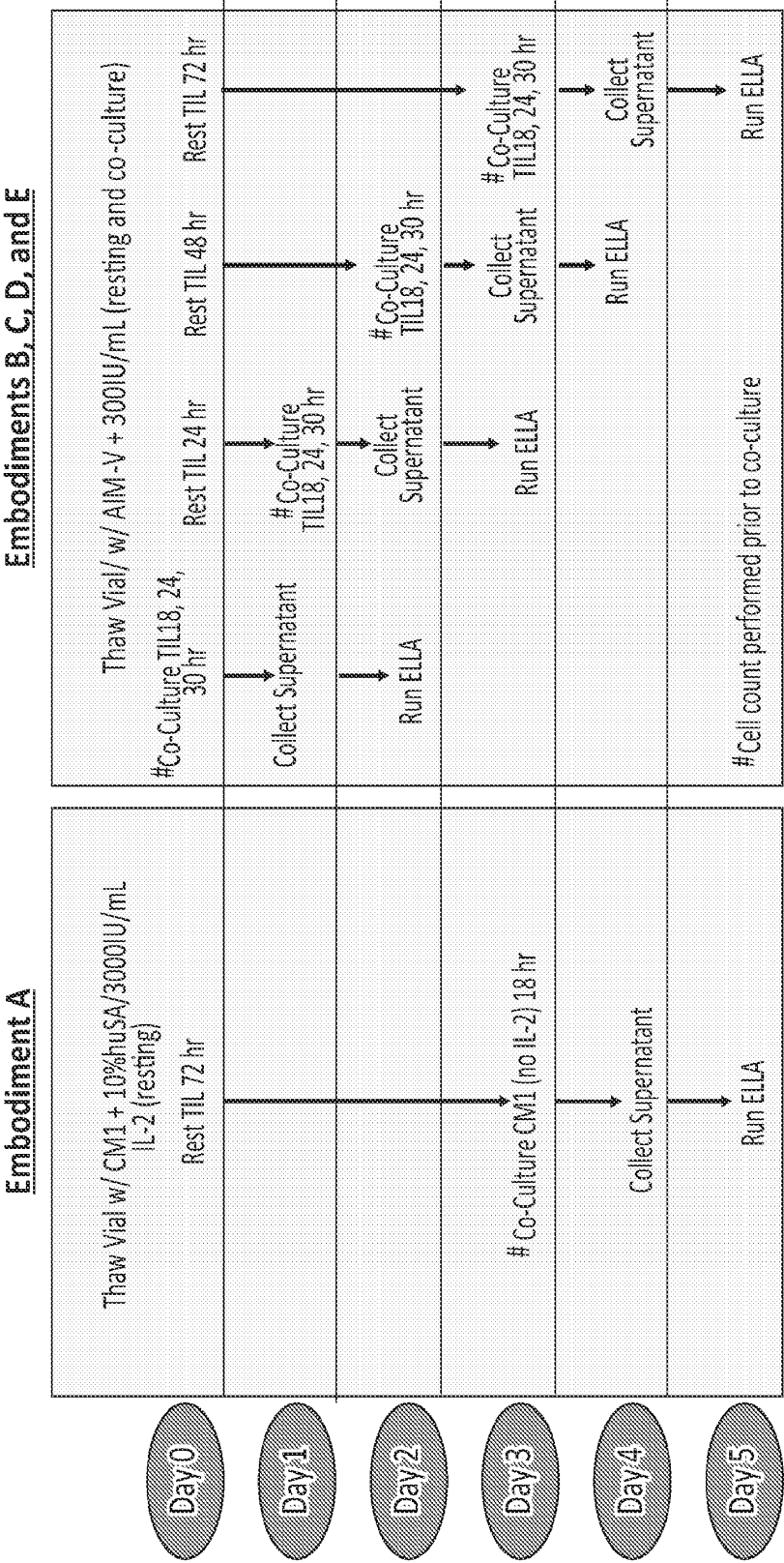


Figure 112

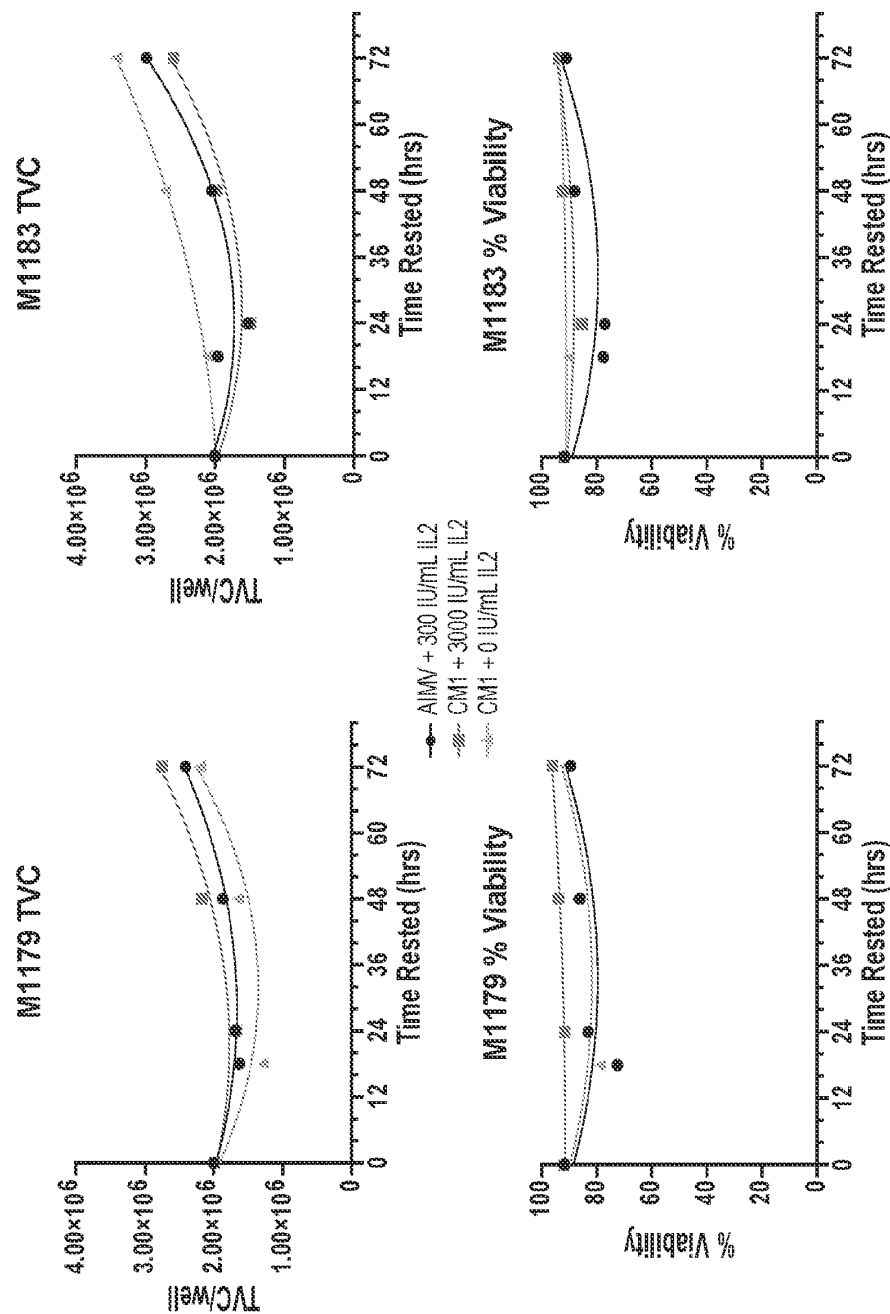


Figure 113

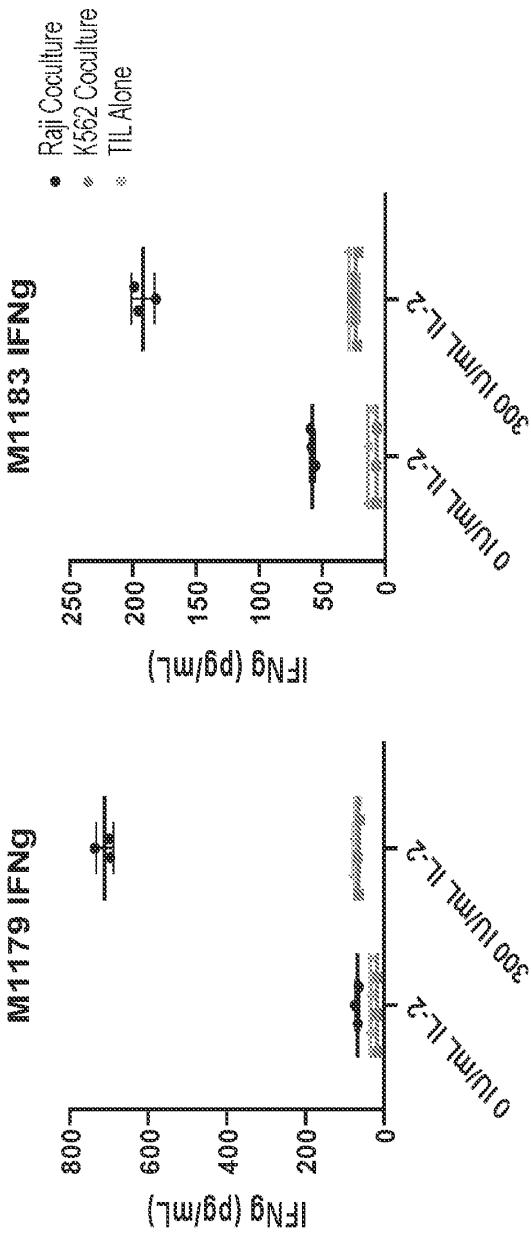


Figure 114

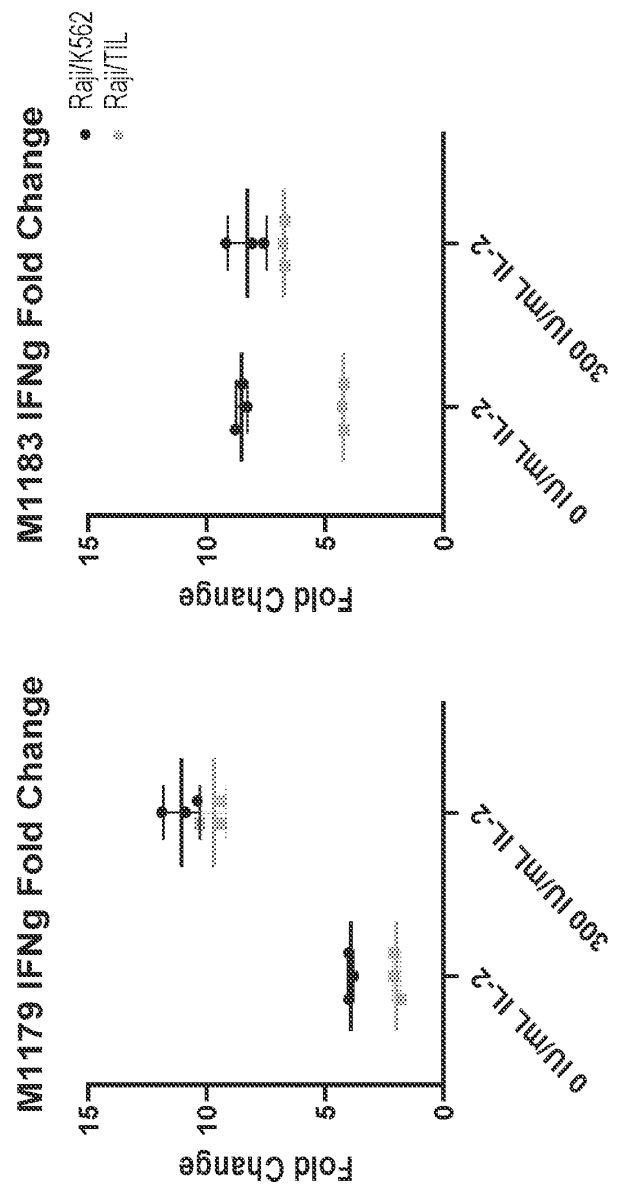


Figure 115

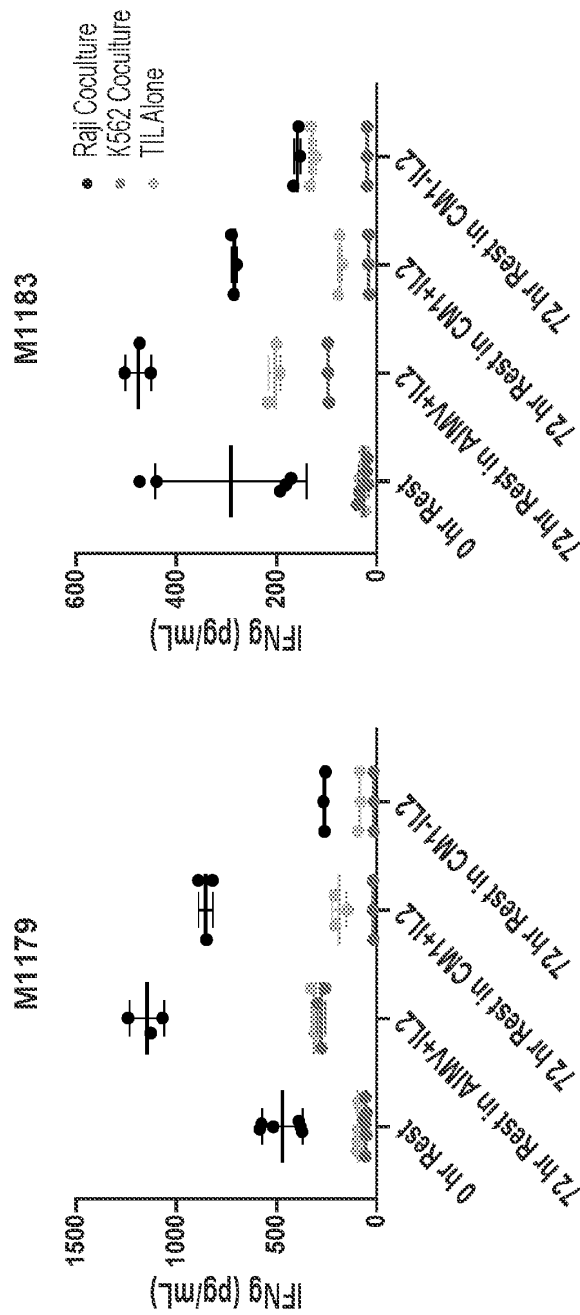


Figure 116

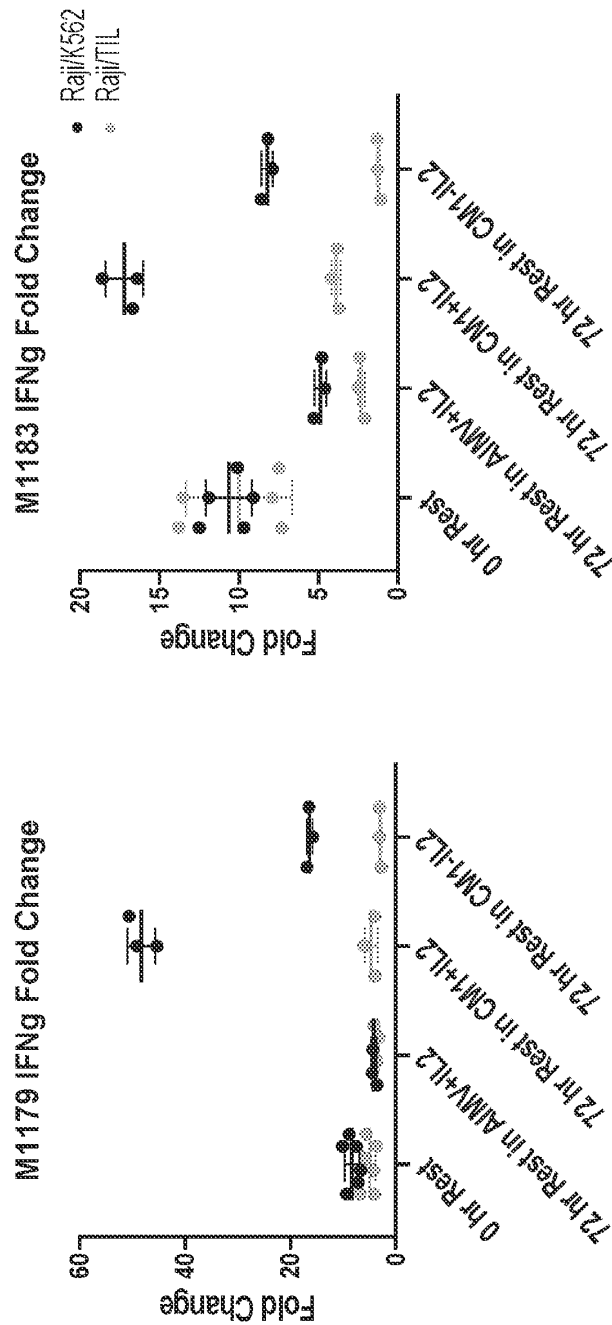


Figure 117

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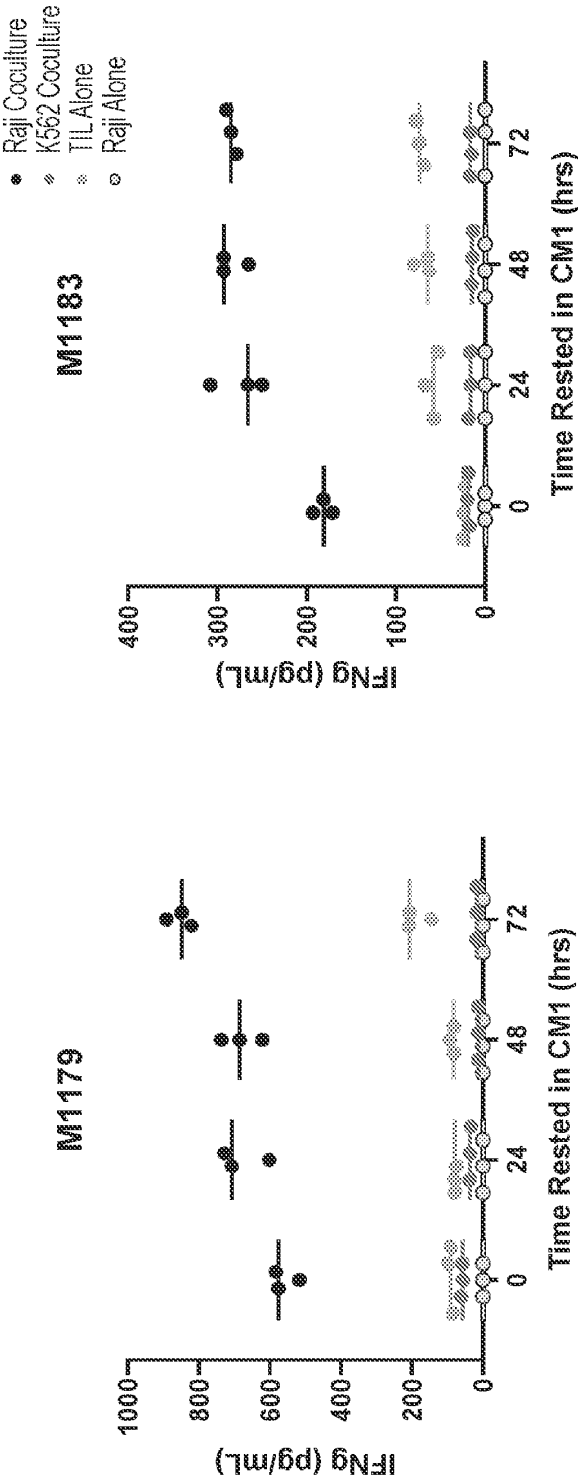


Figure 118

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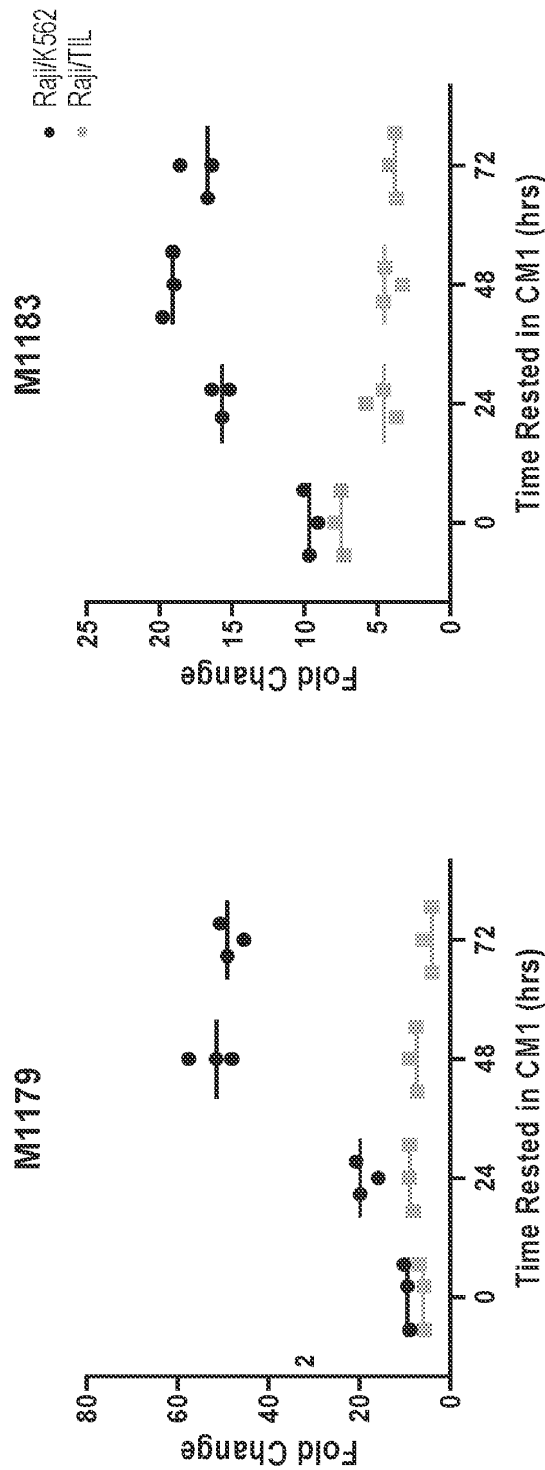


Figure 119

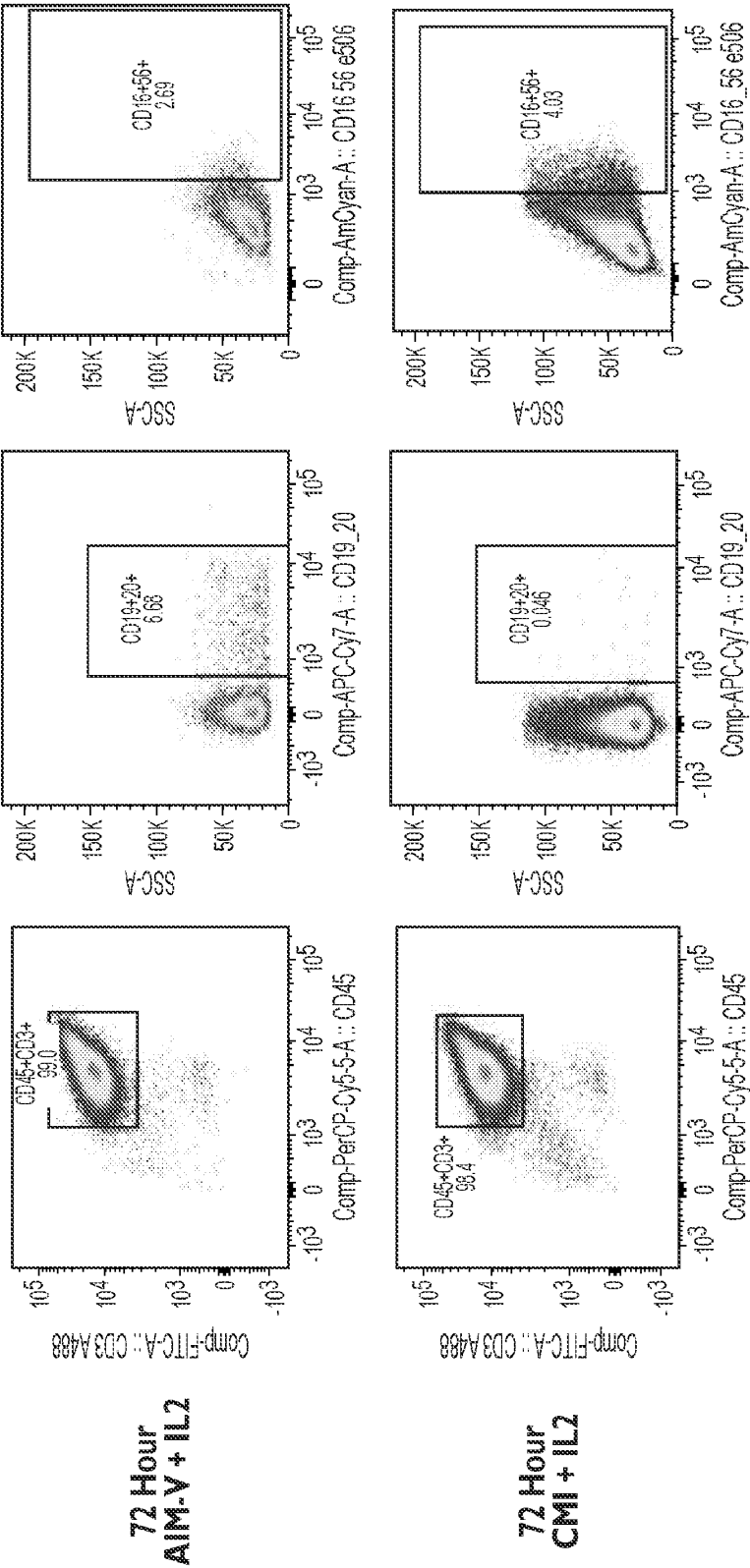


Figure 120

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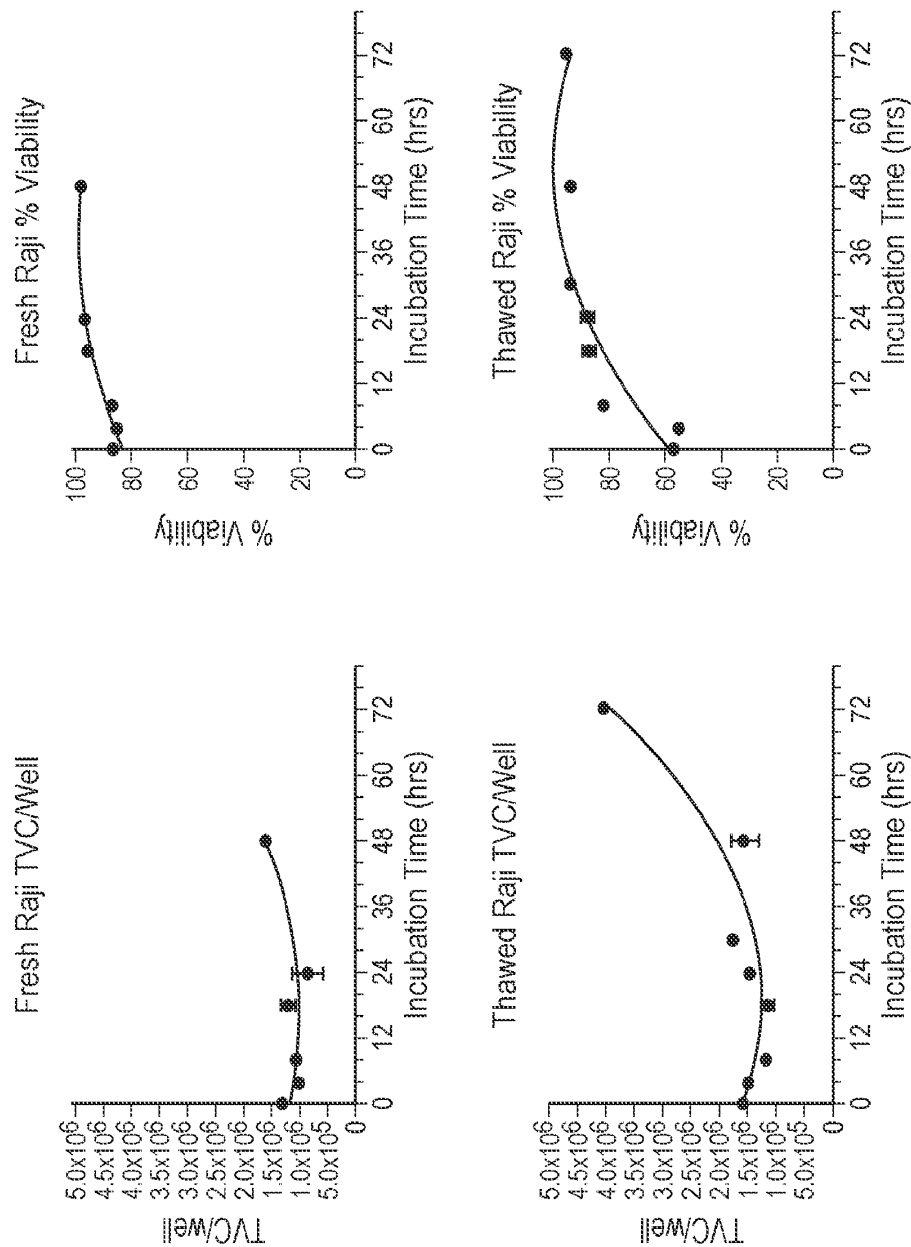


Figure 121

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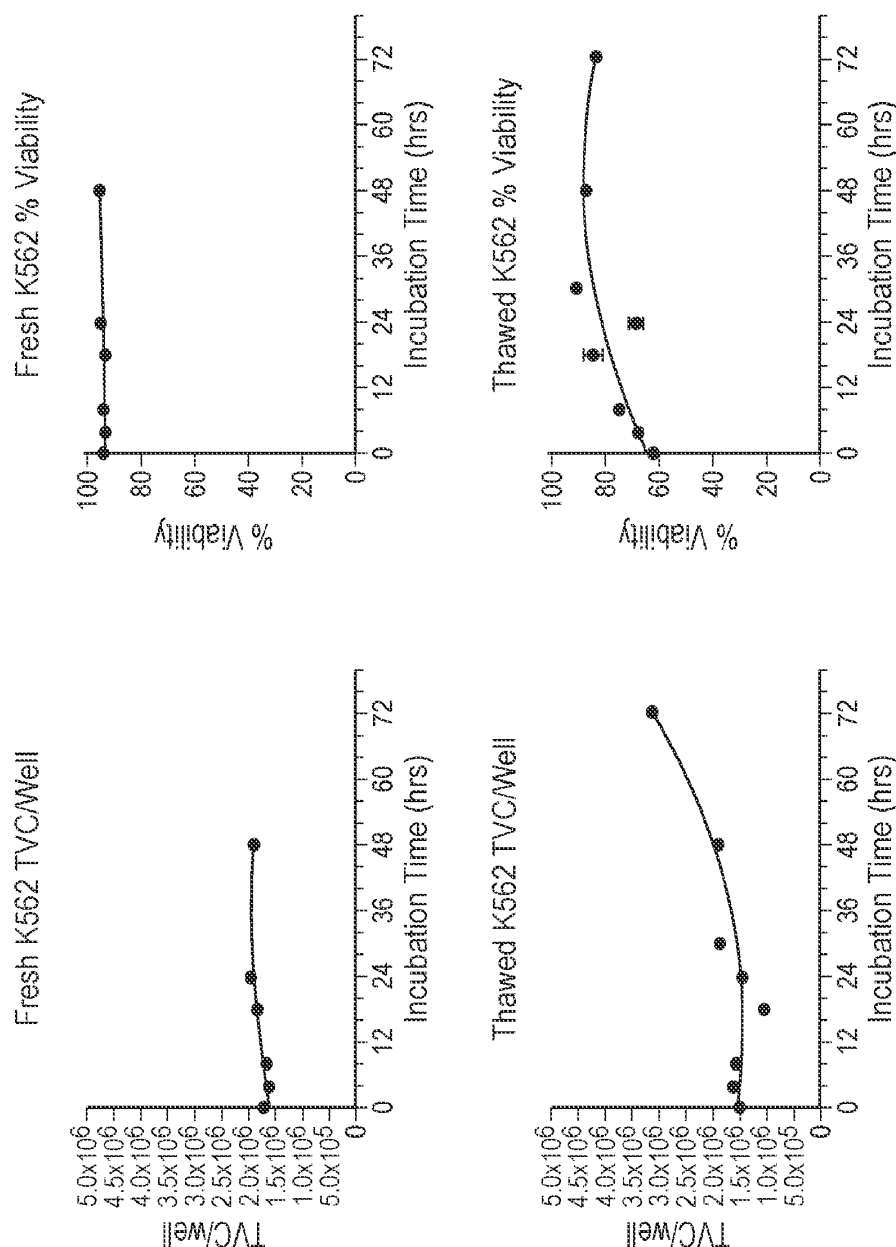


Figure 122

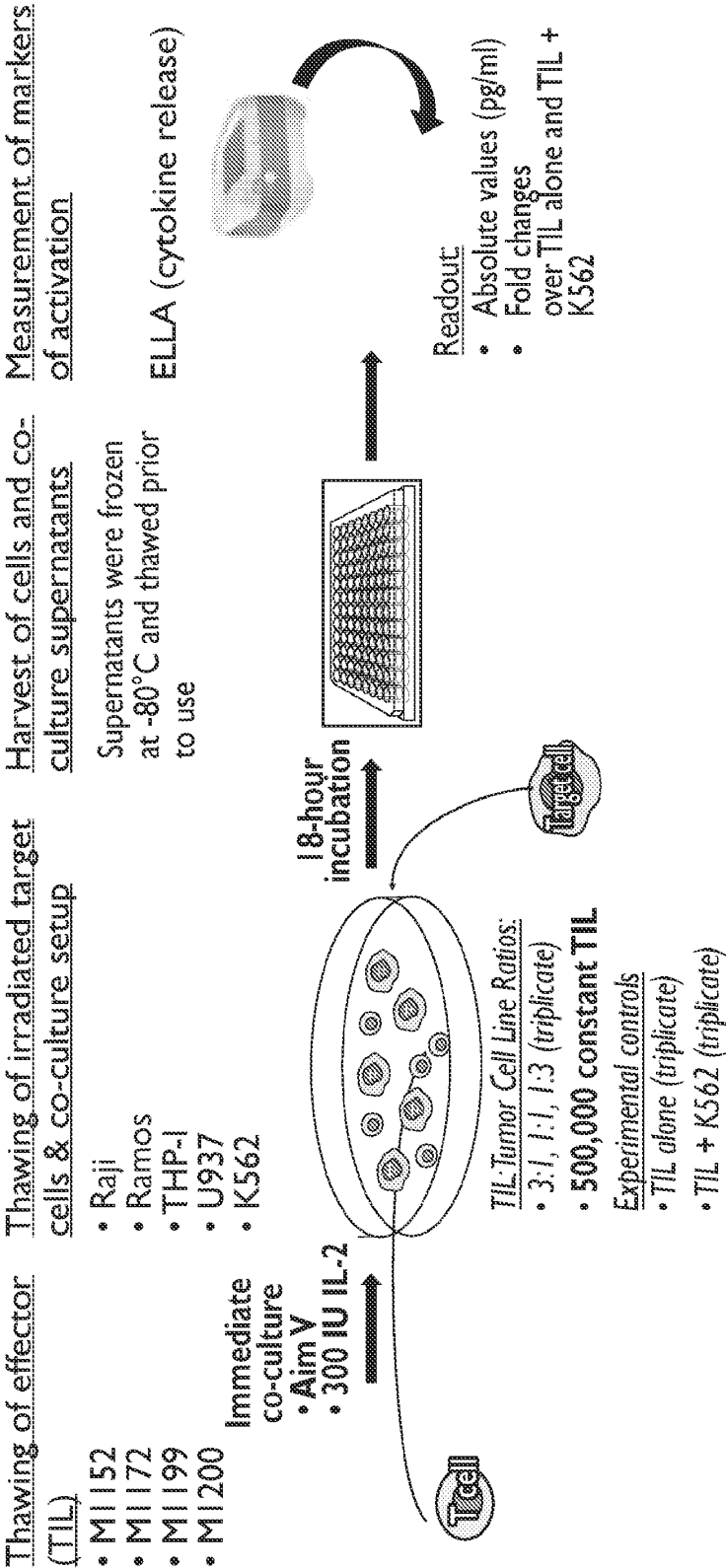


Figure 123

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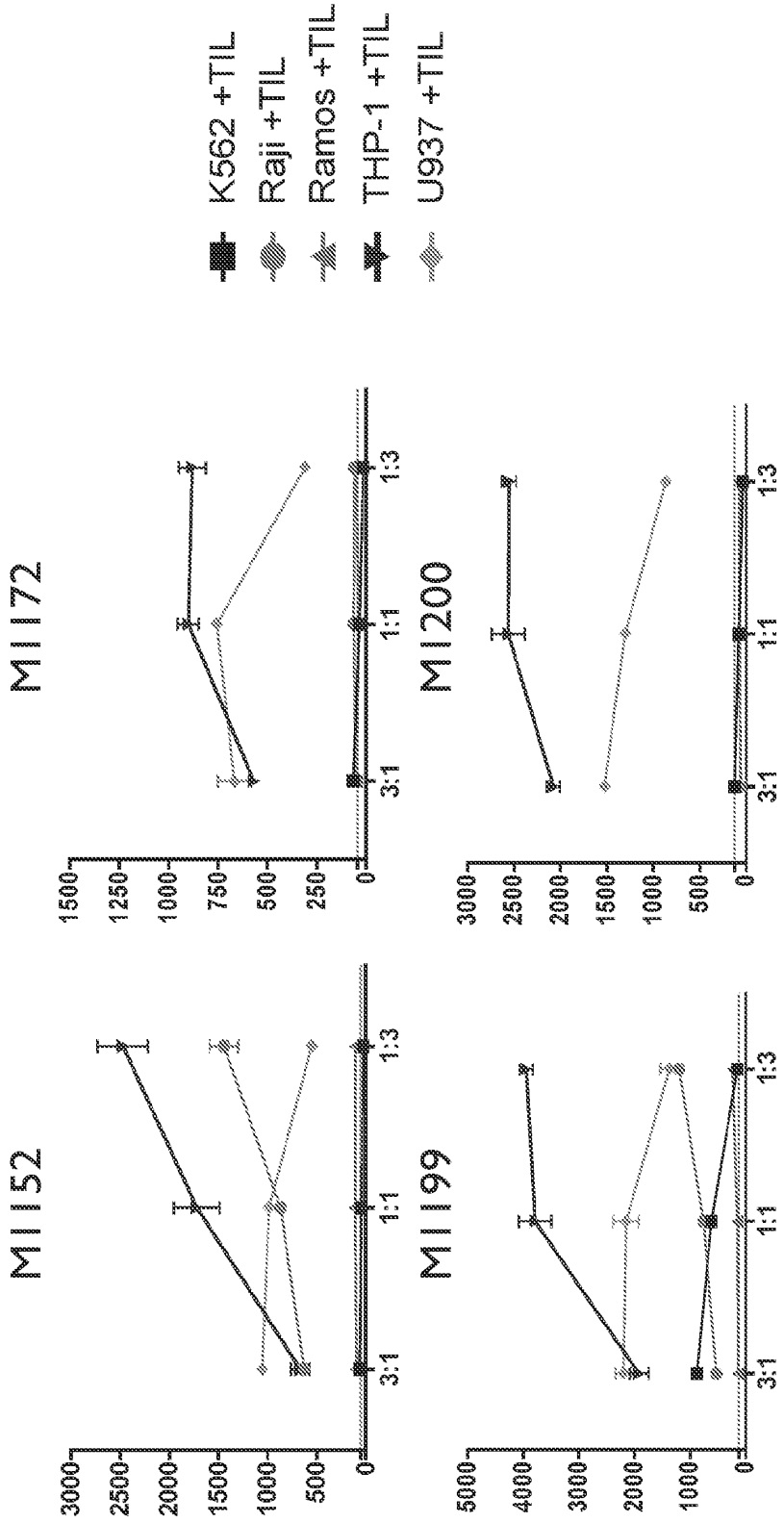


Figure 124

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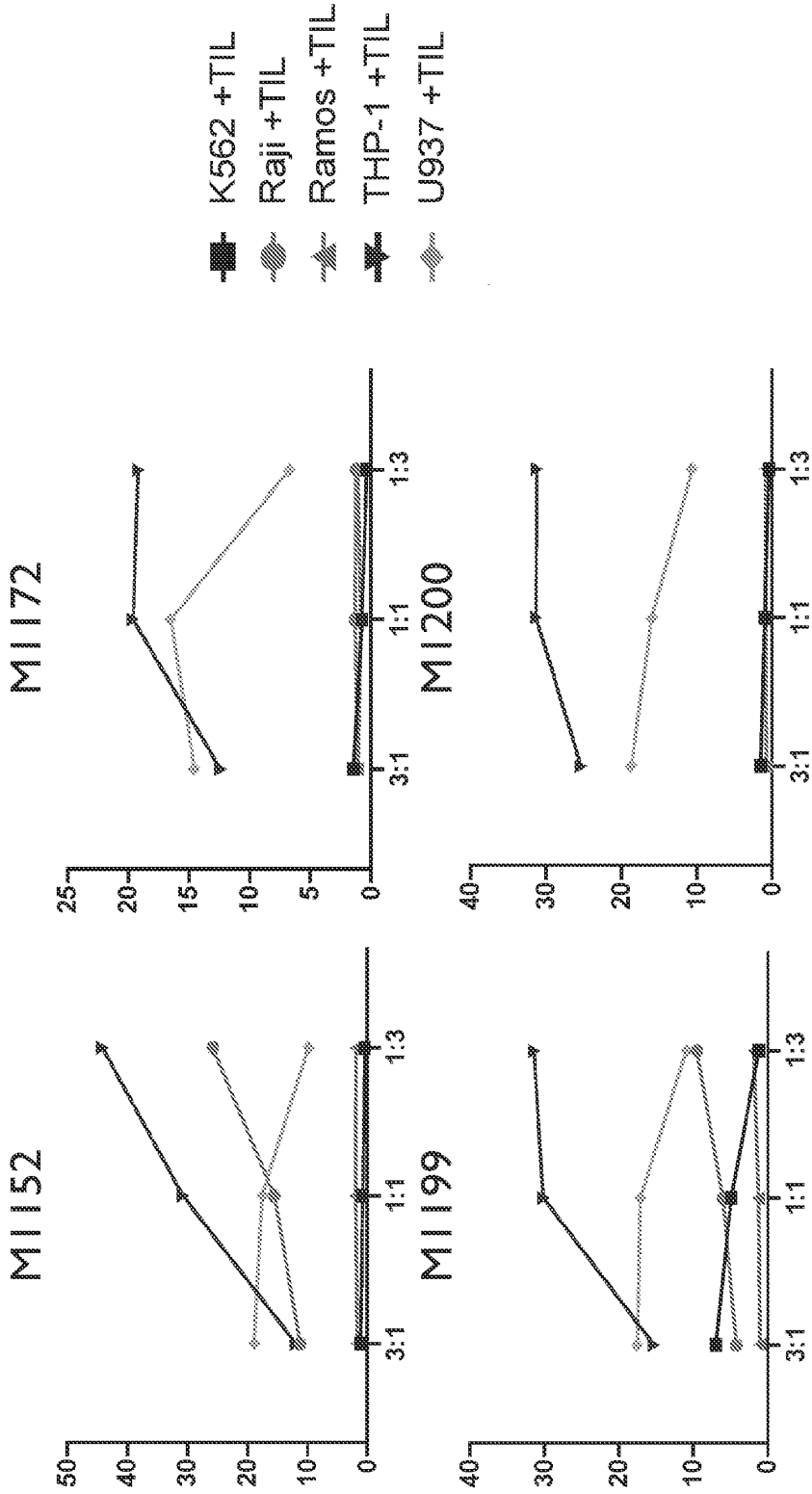


Figure 125

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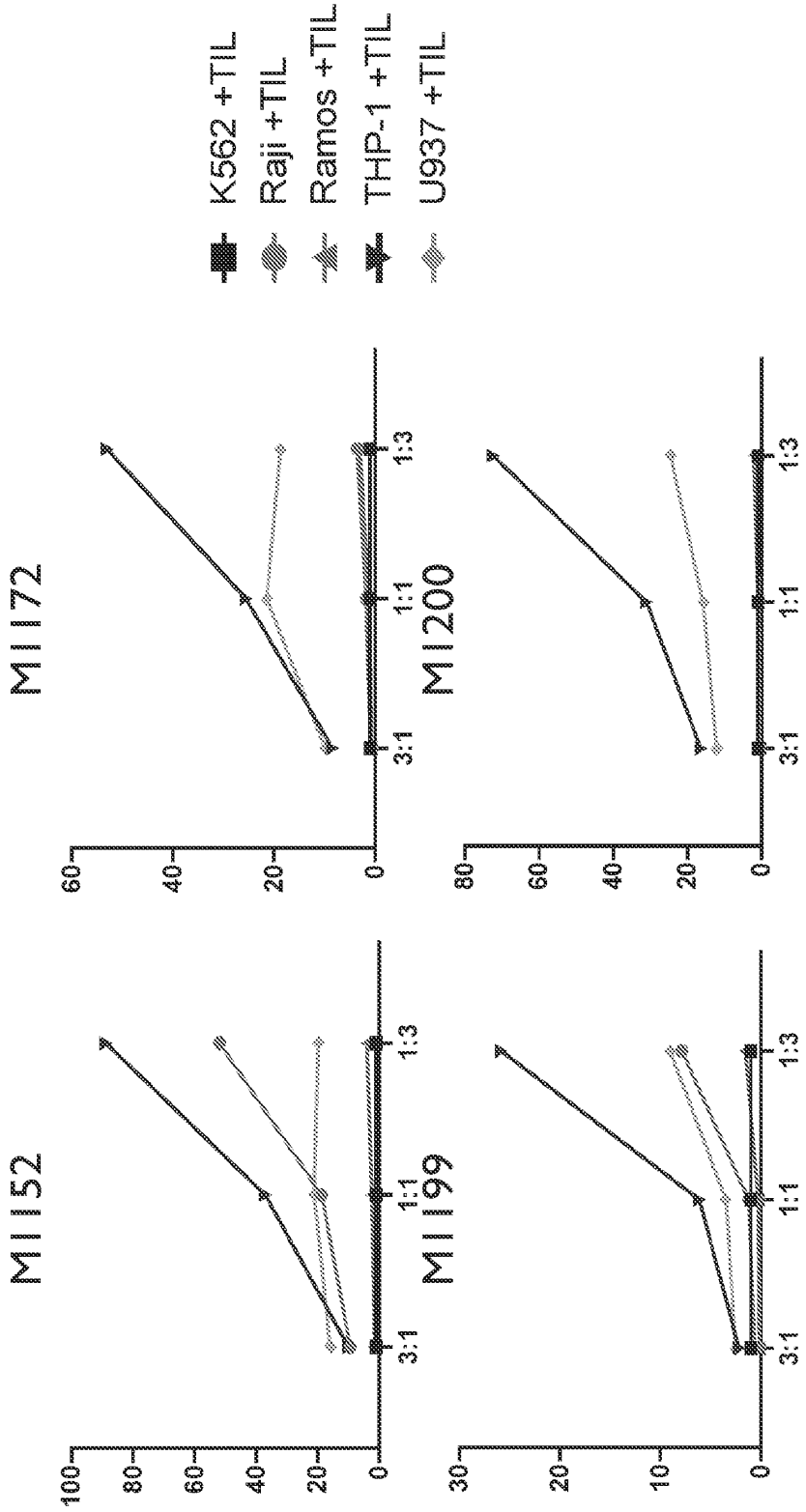


Figure 126

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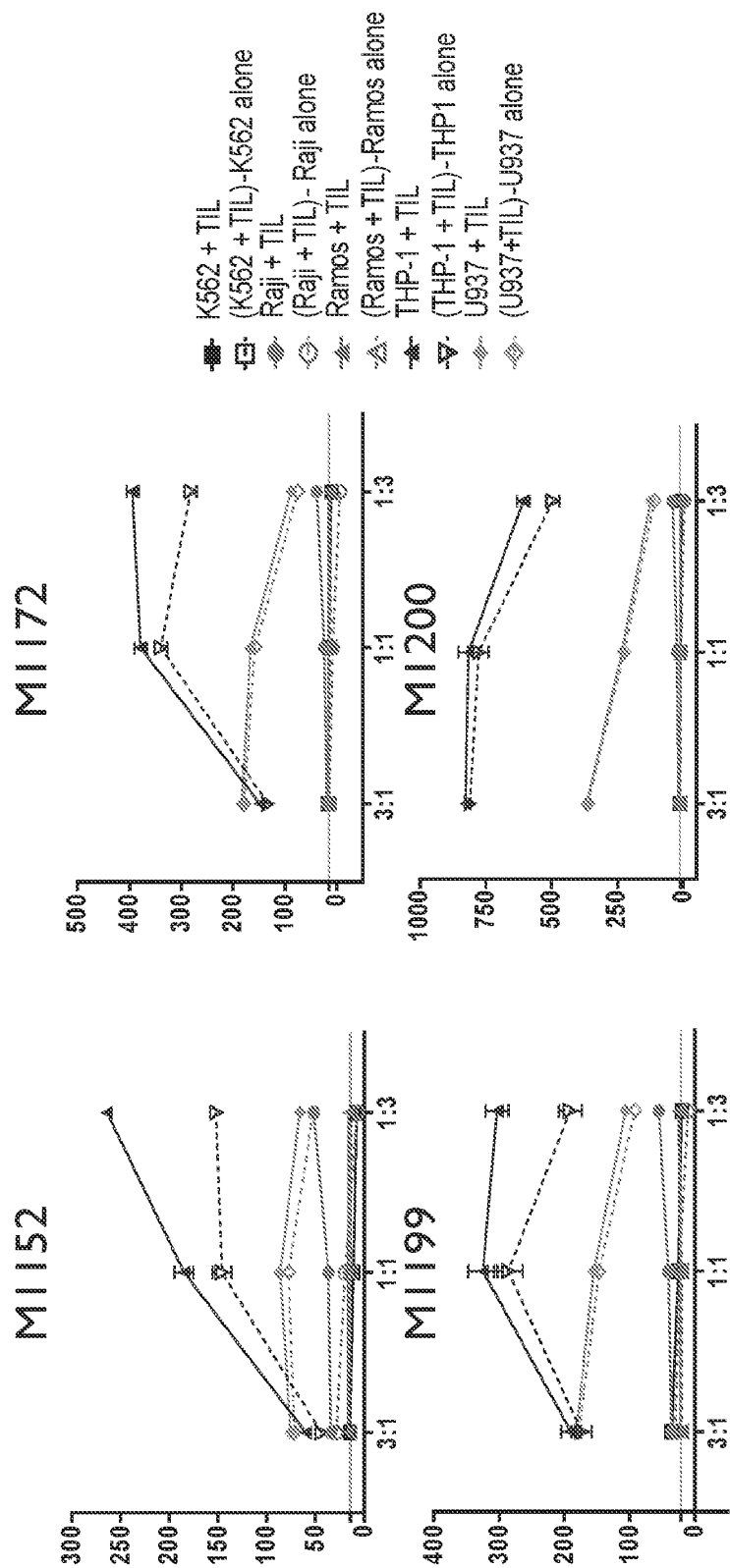


Figure 127

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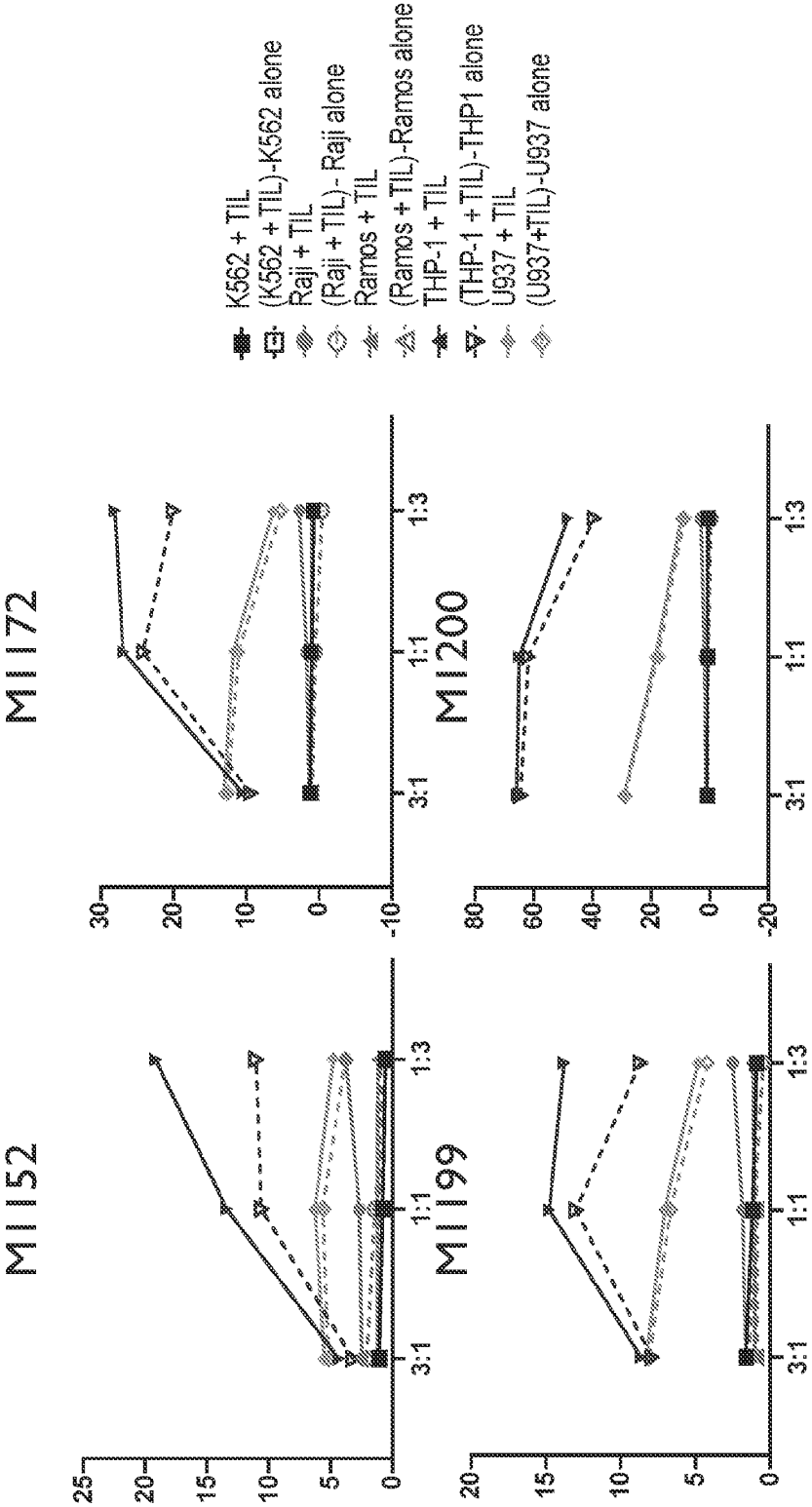


Figure 128

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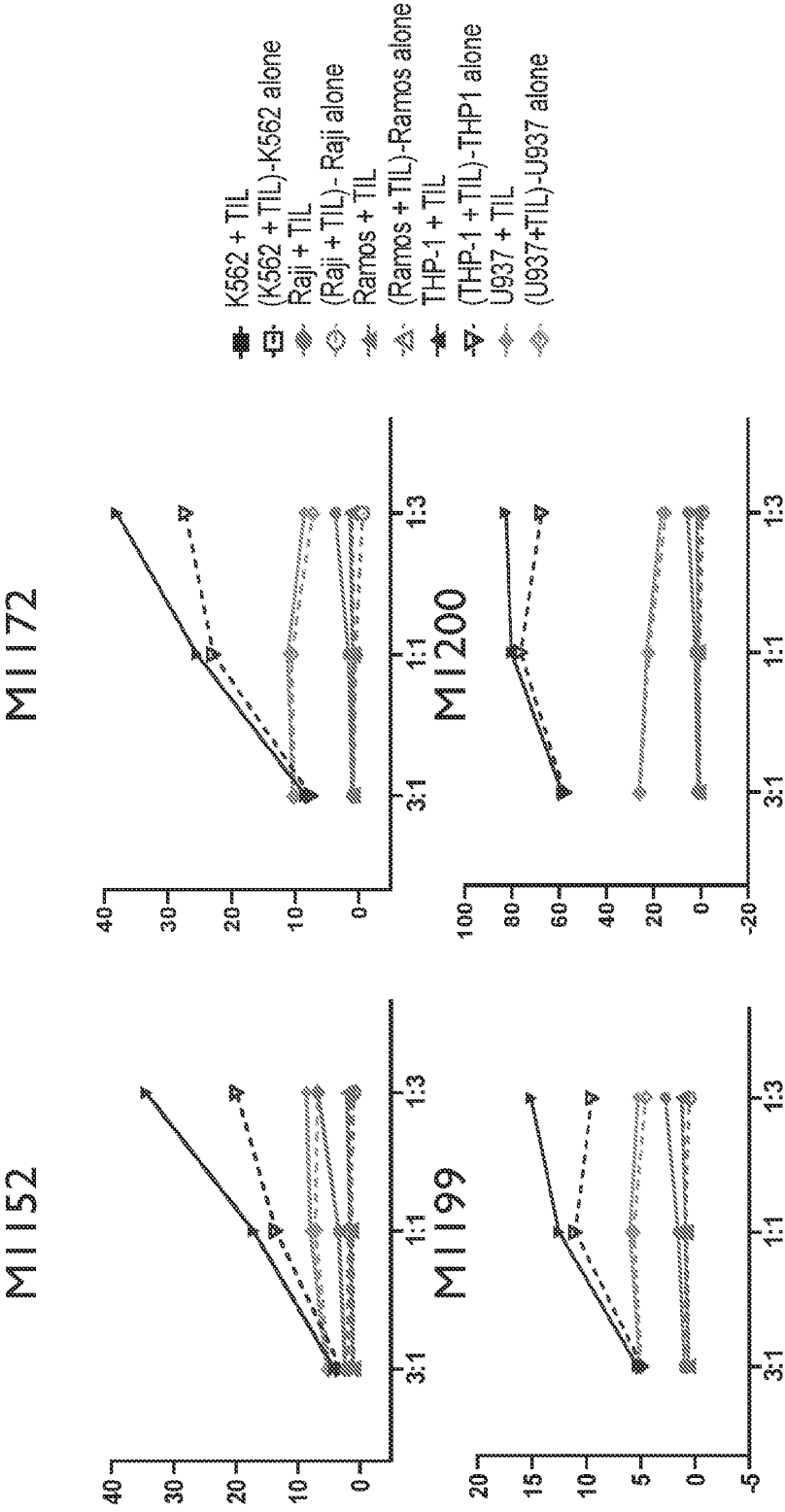


Figure 129

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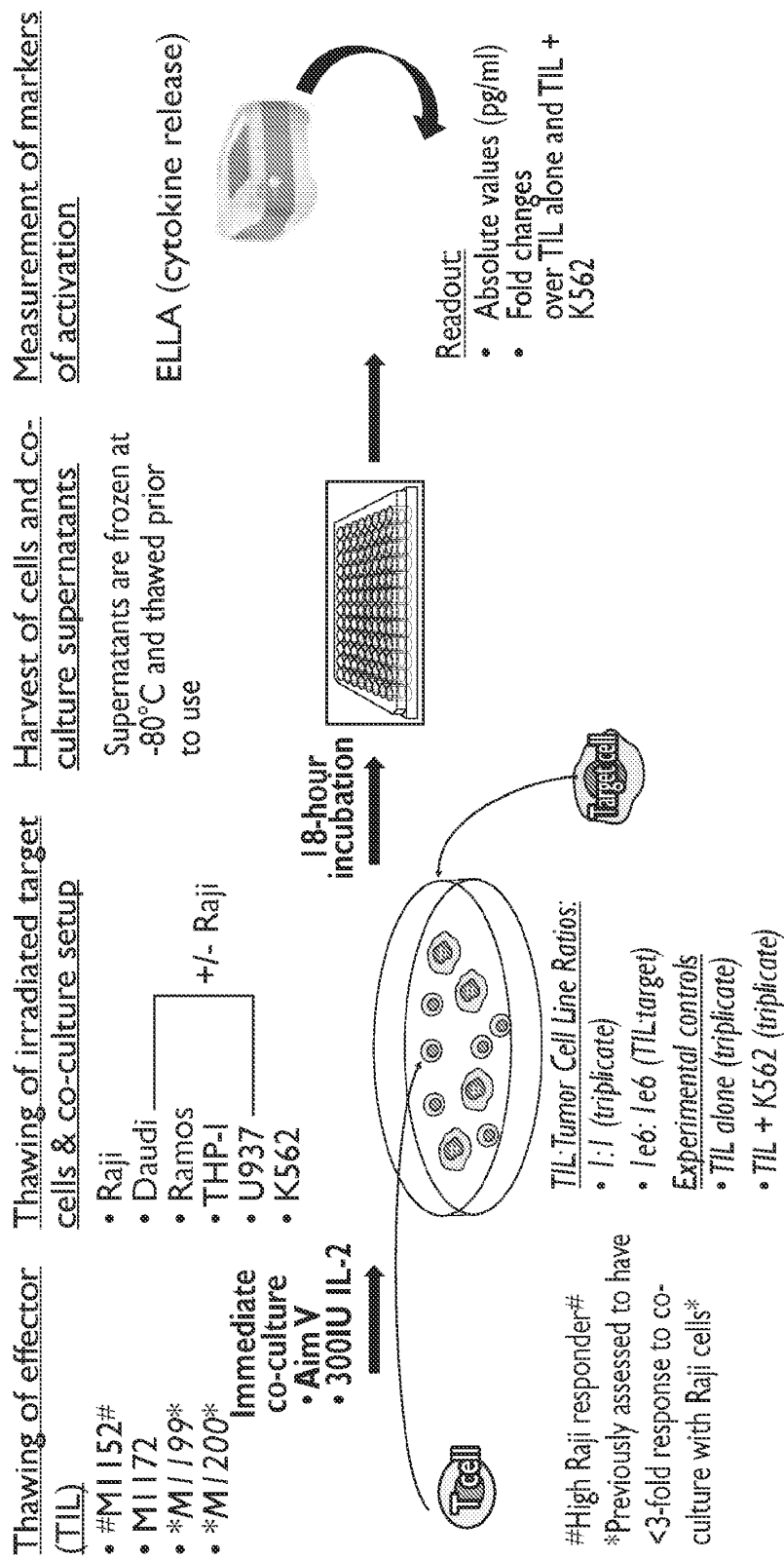


Figure 130

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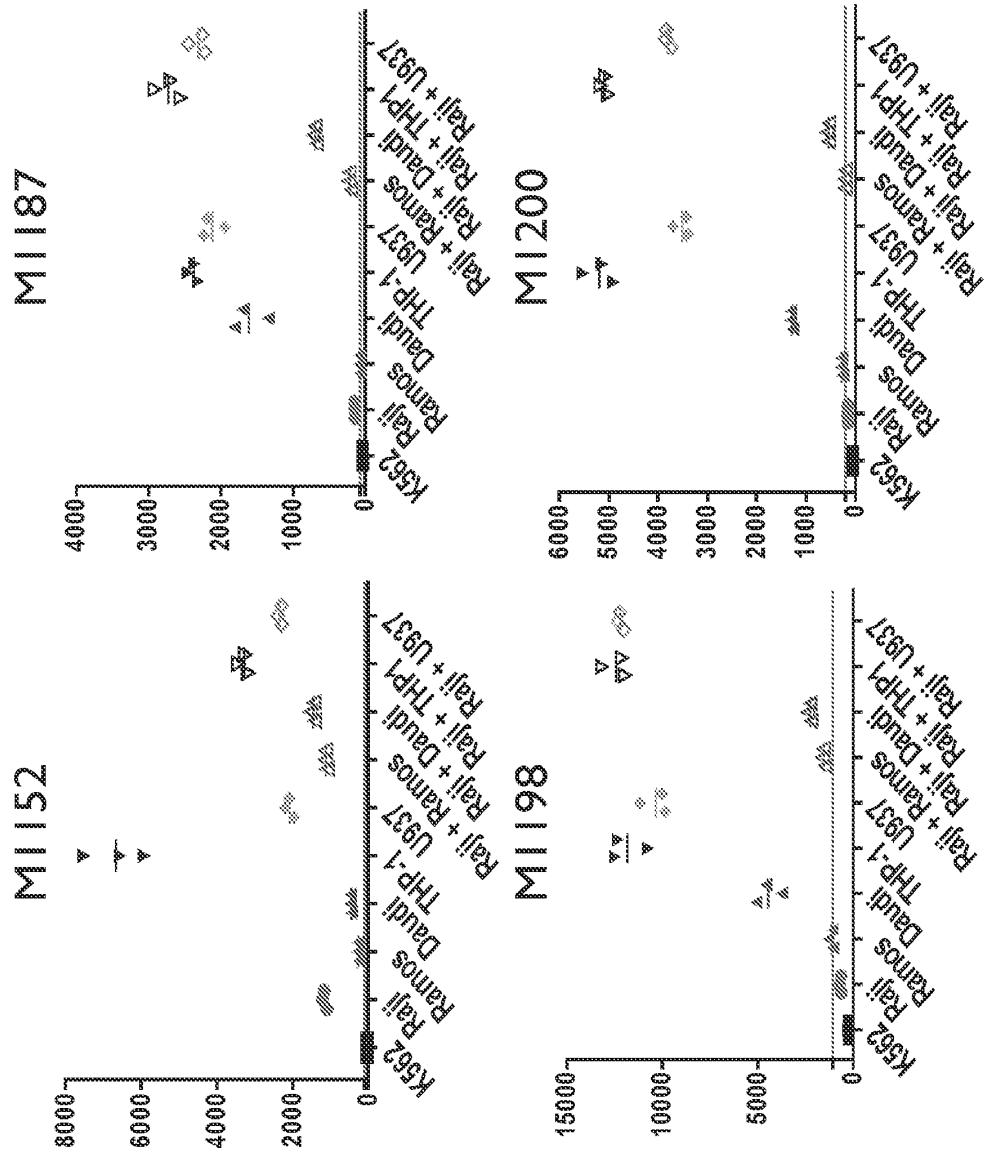


Figure 131

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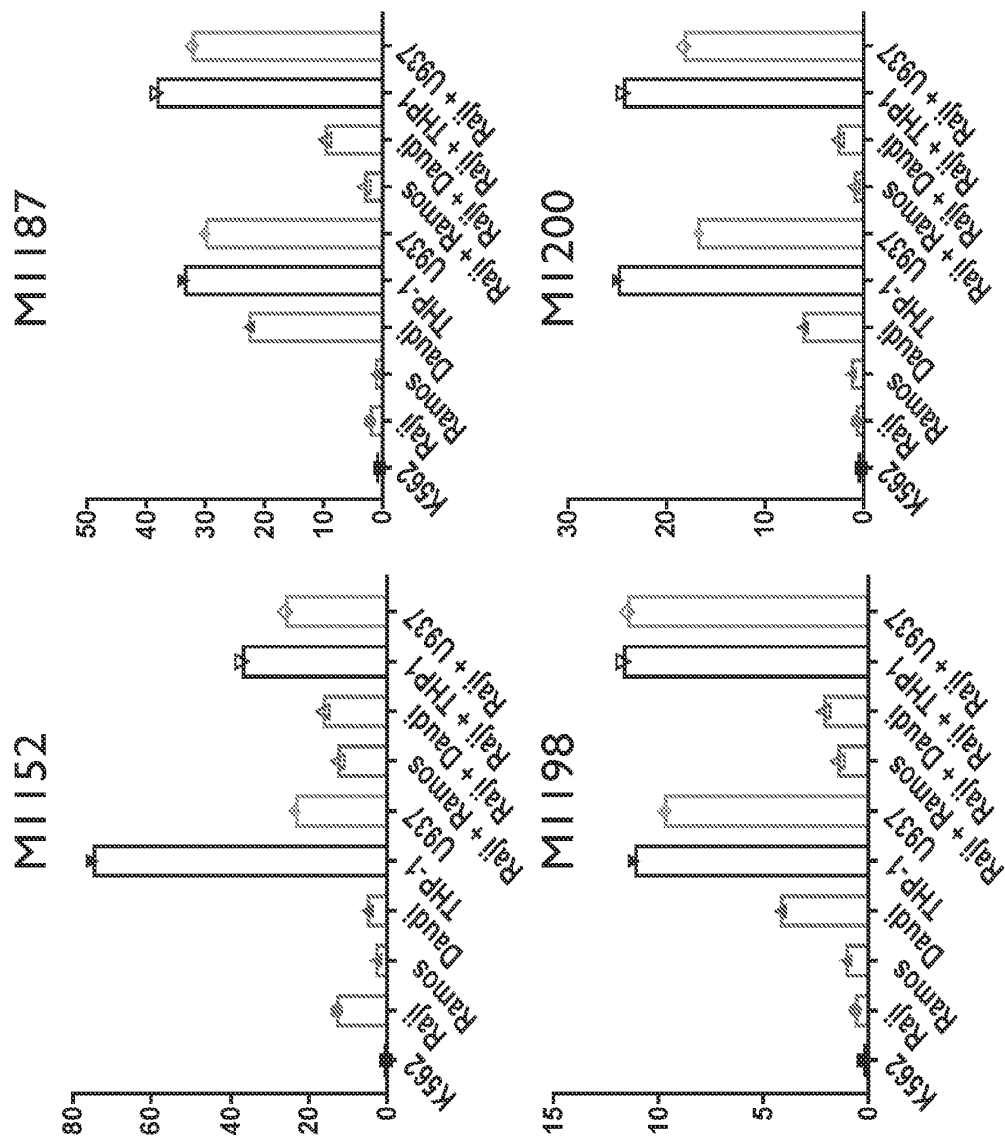


Figure 132

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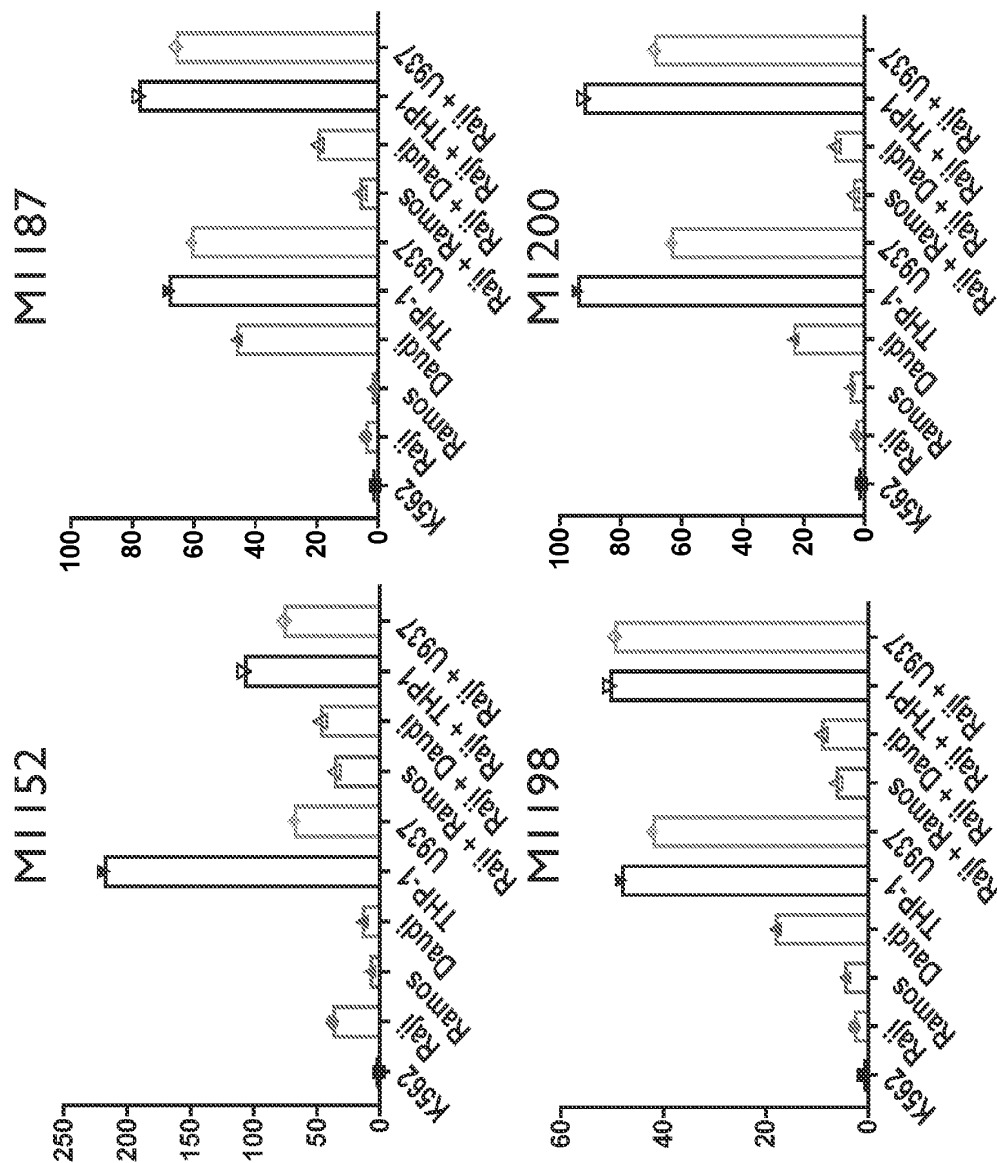


Figure 133

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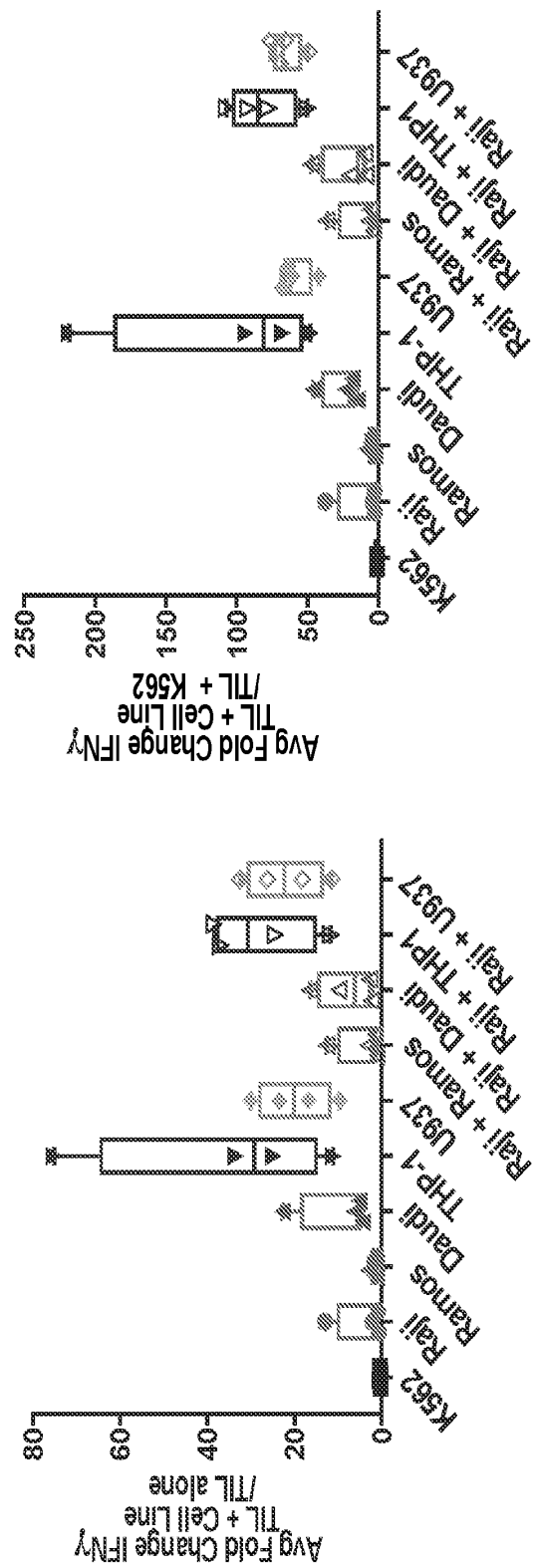


Figure 134

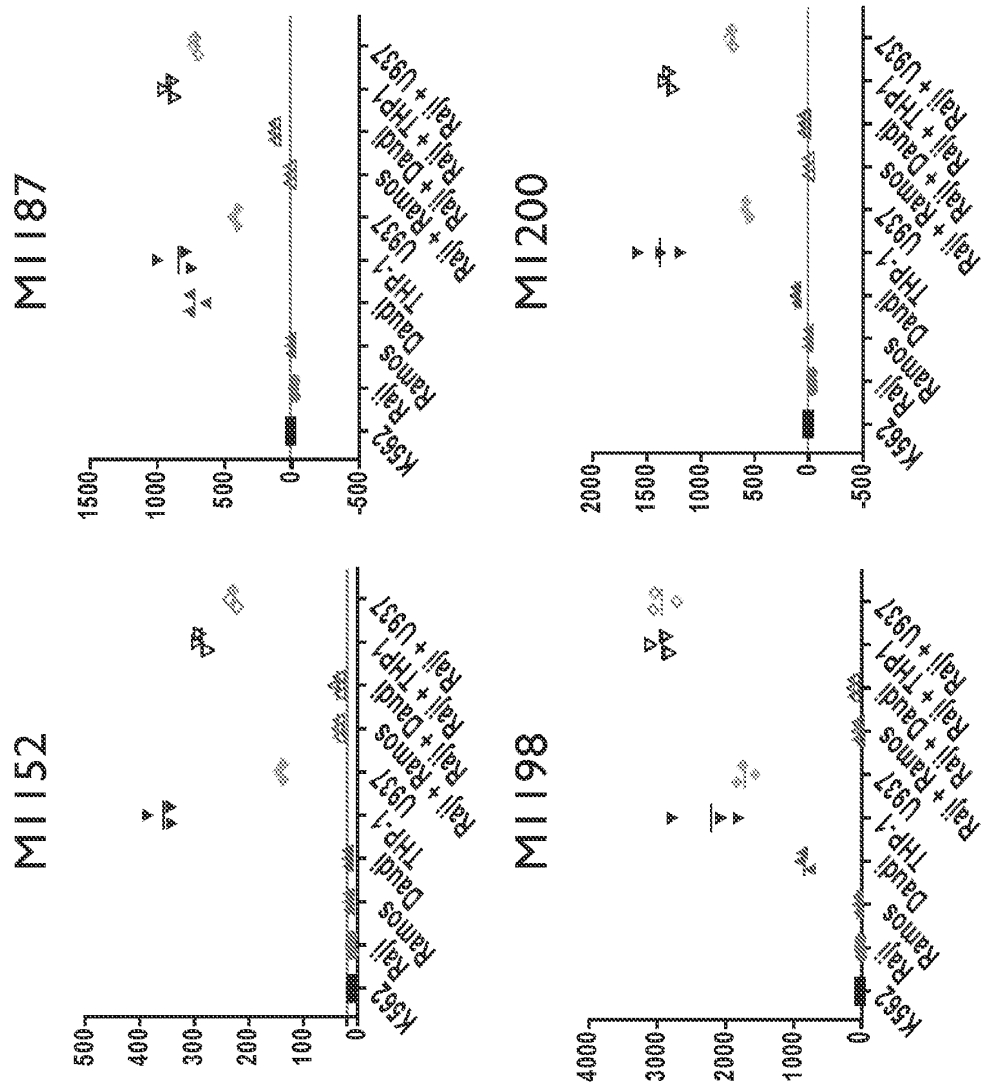


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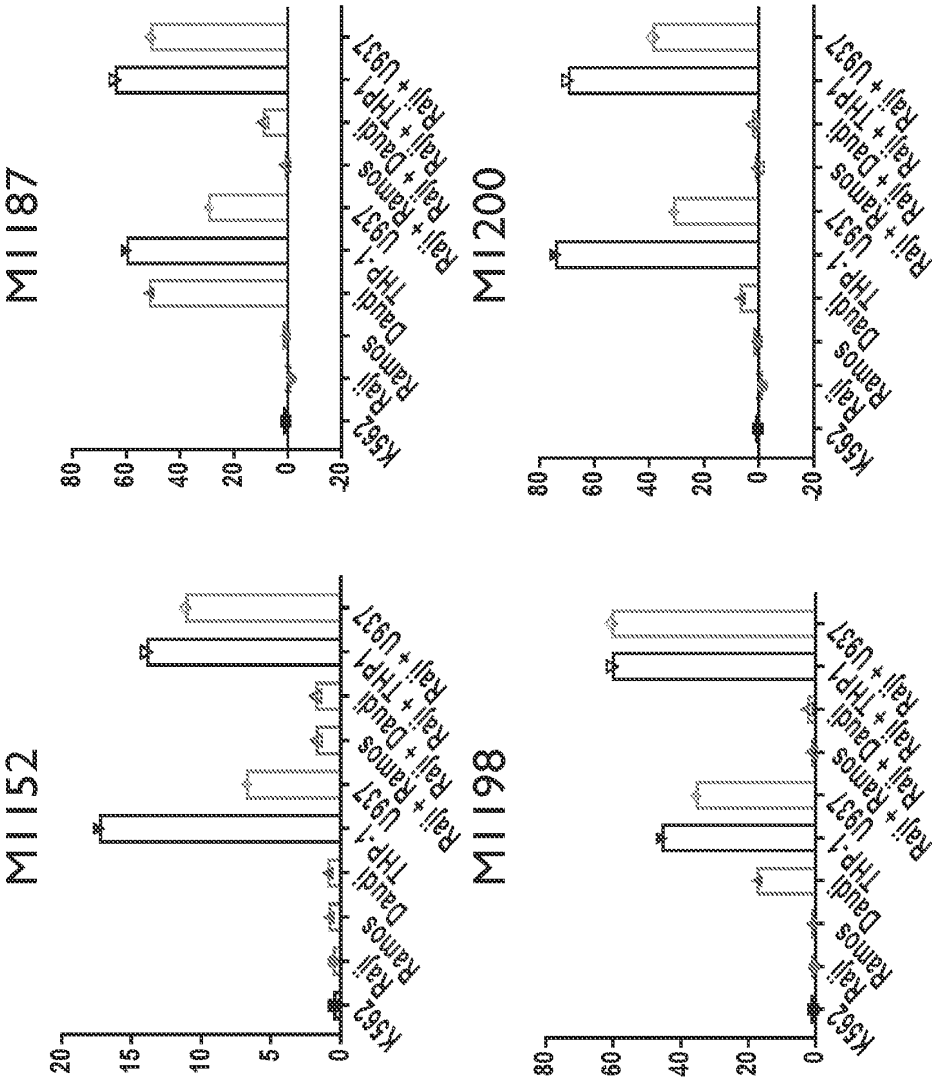


Figure 136

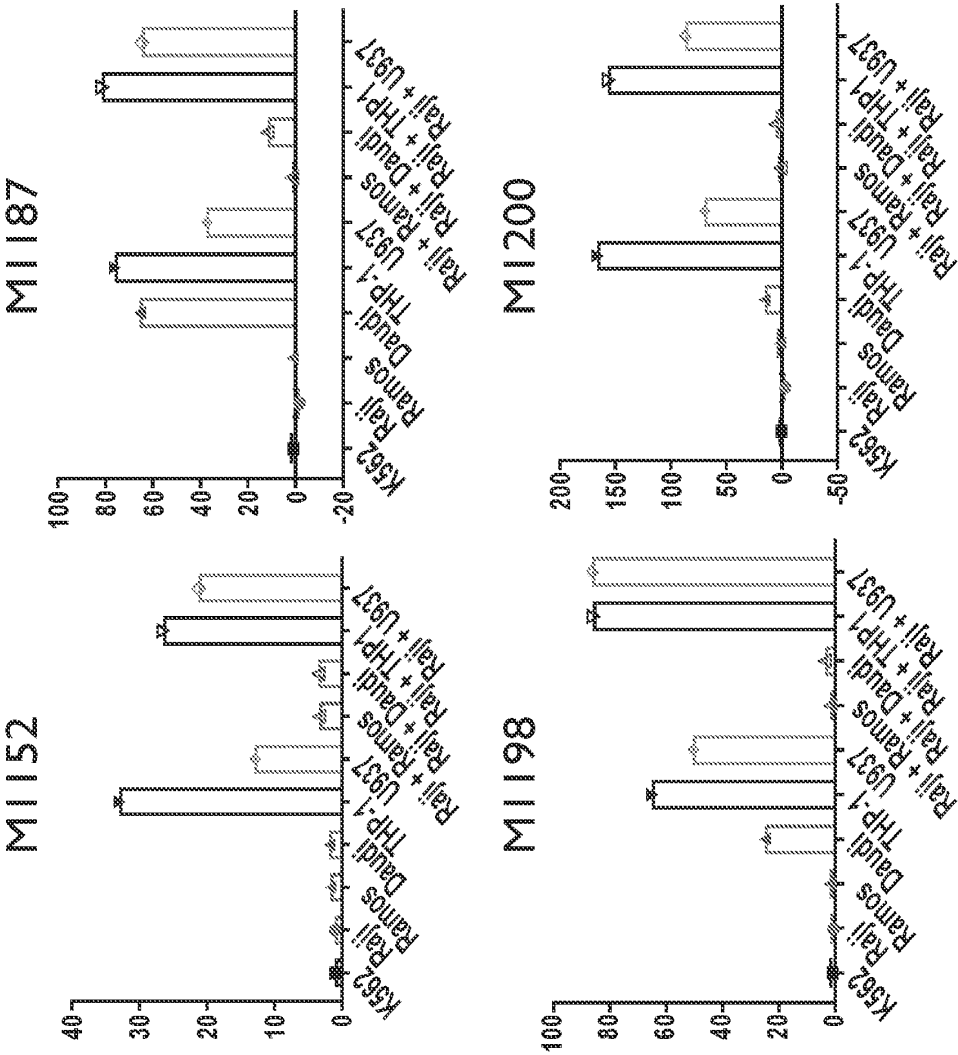


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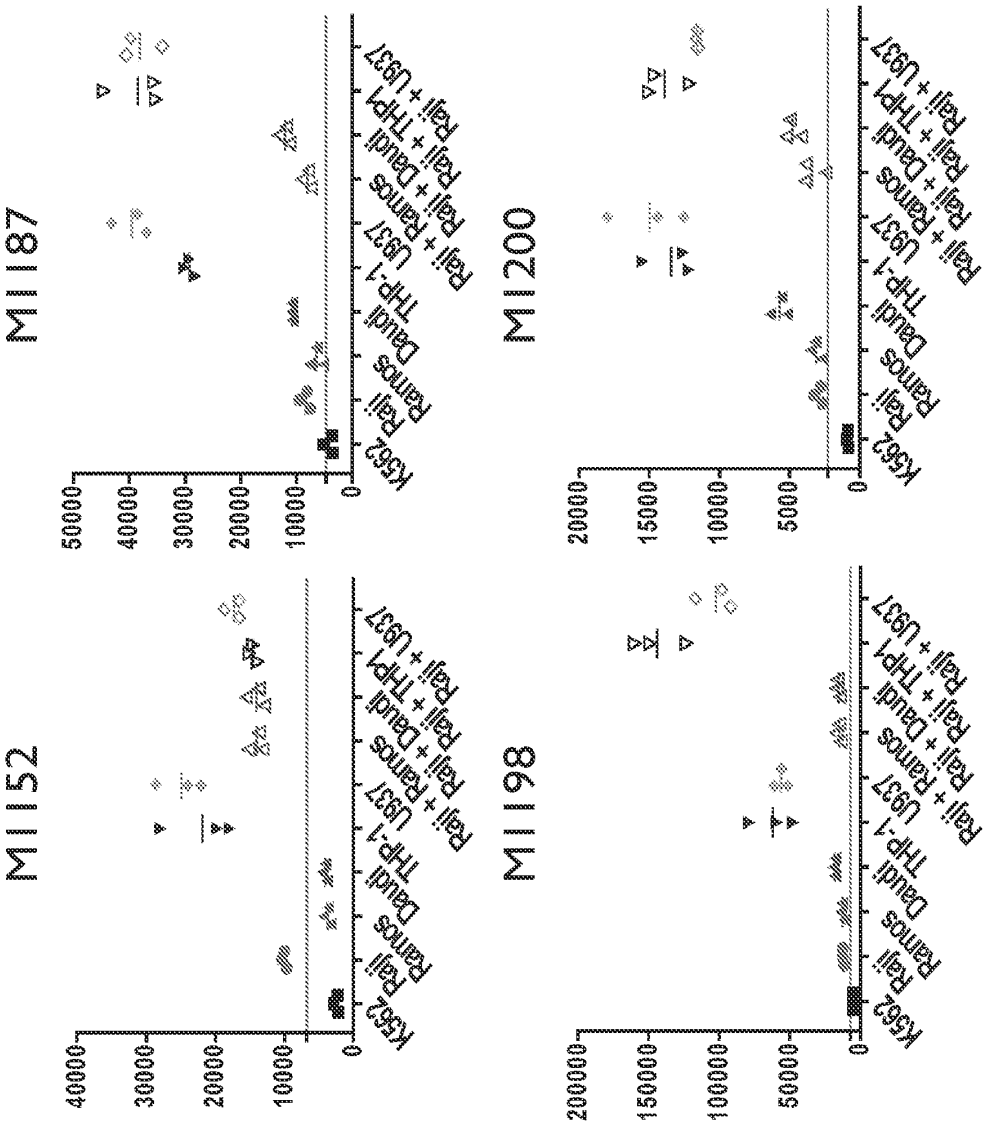
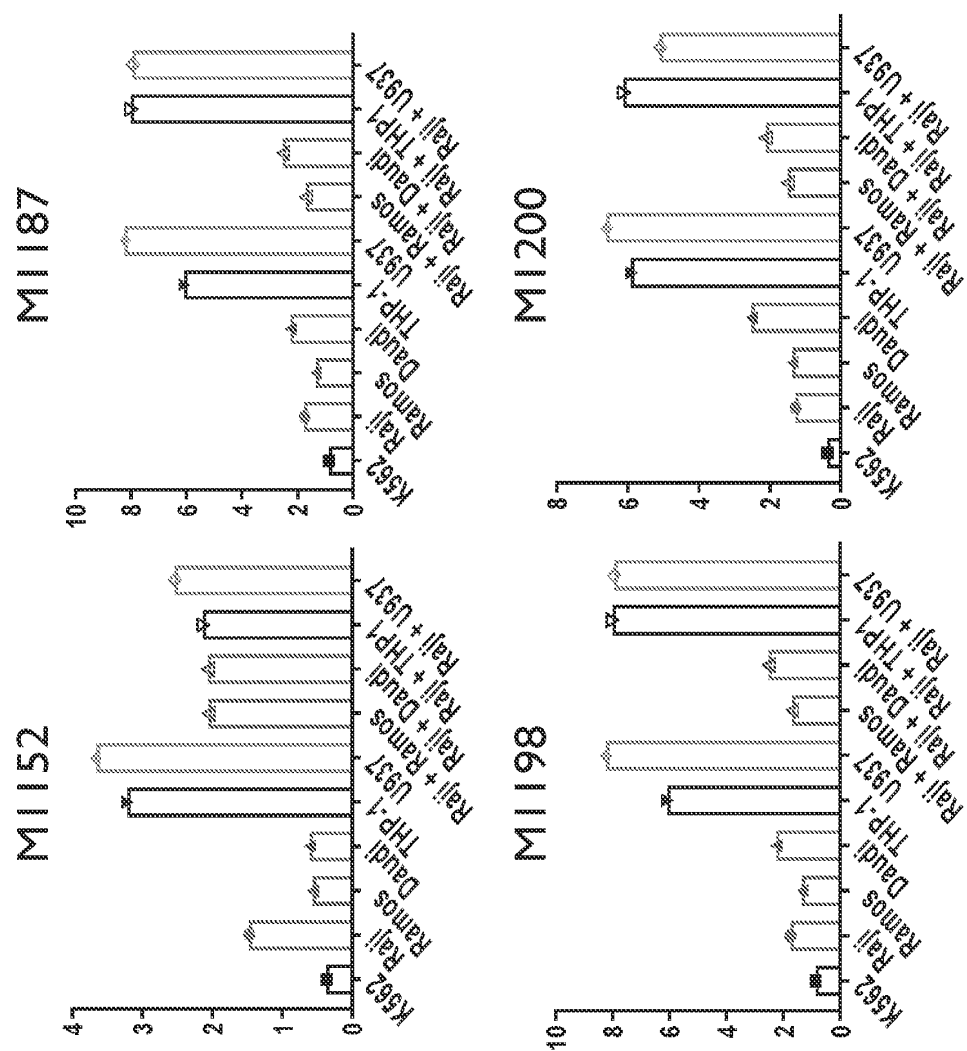


Figure 138



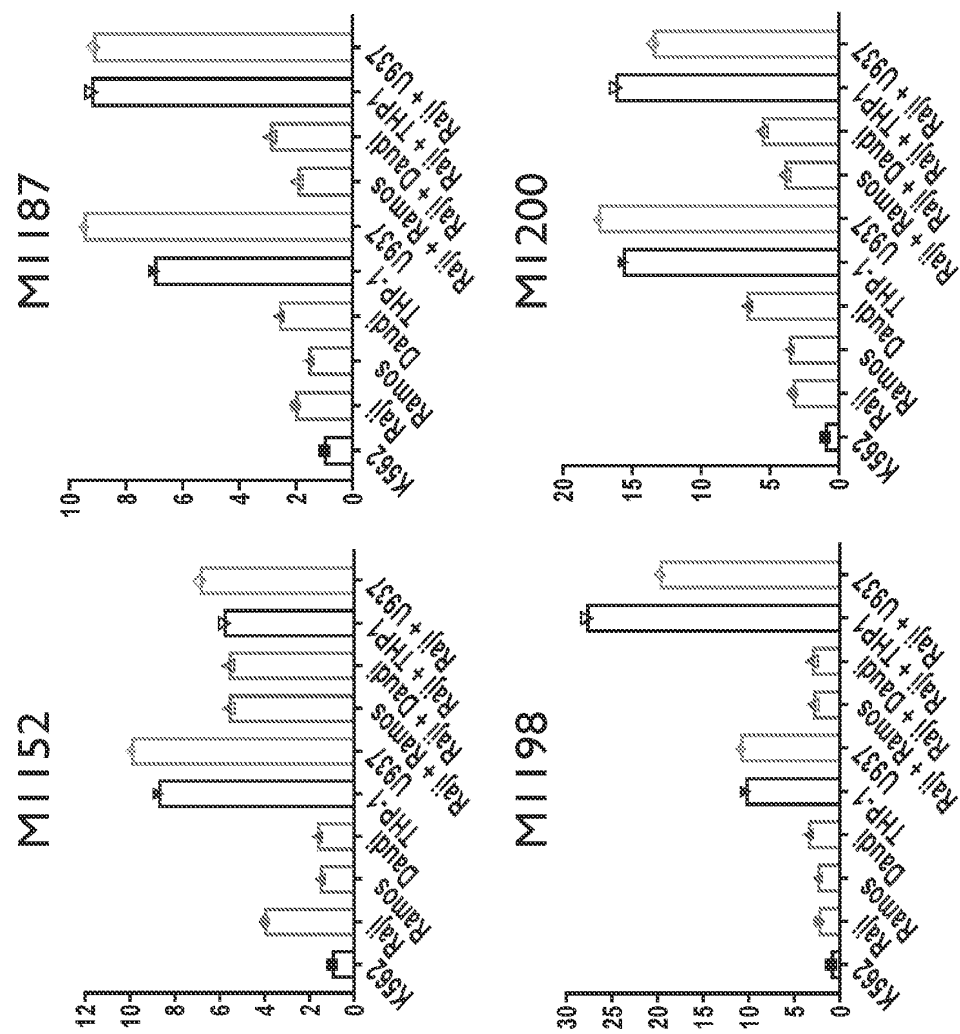


Figure 140

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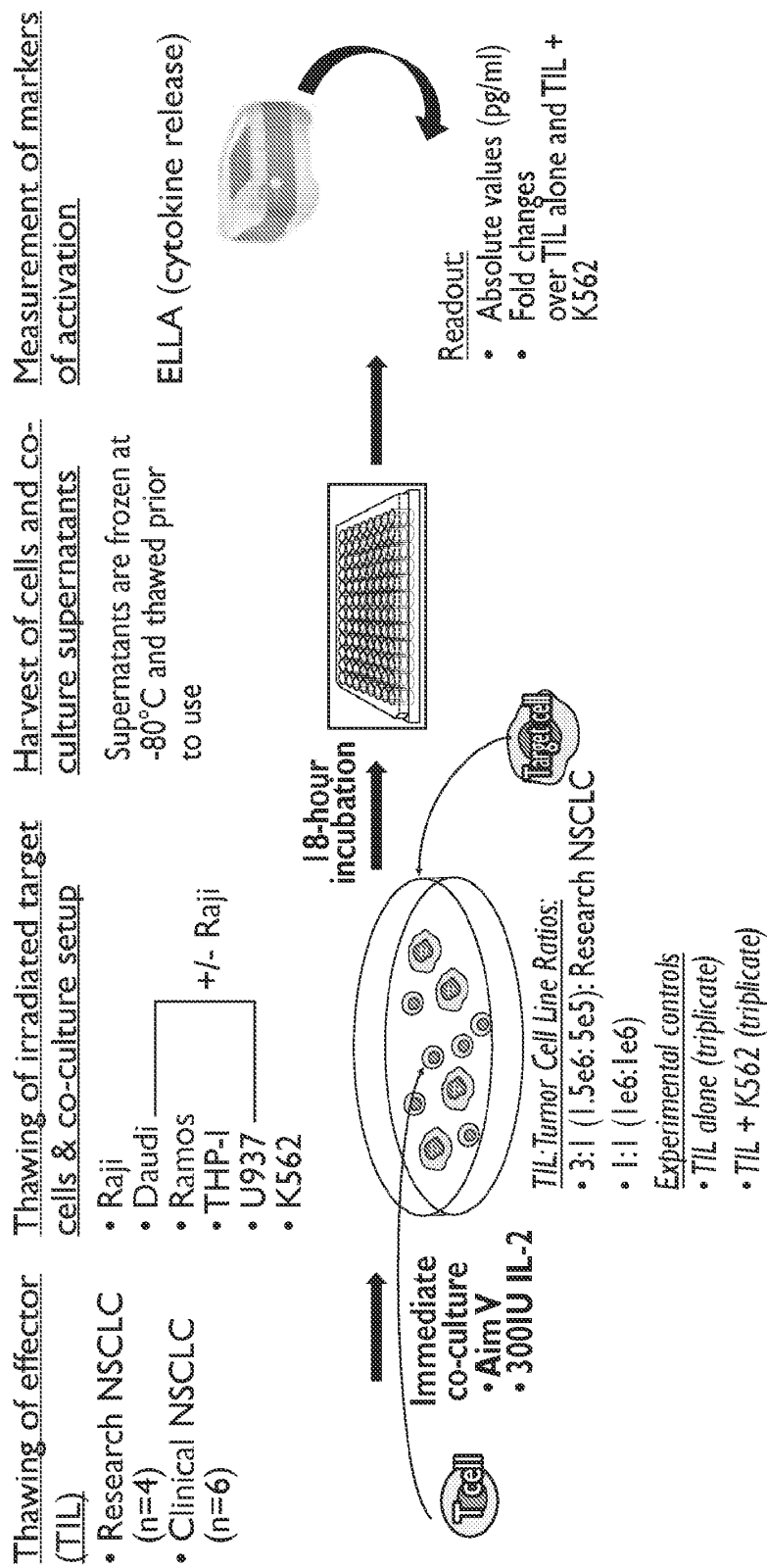


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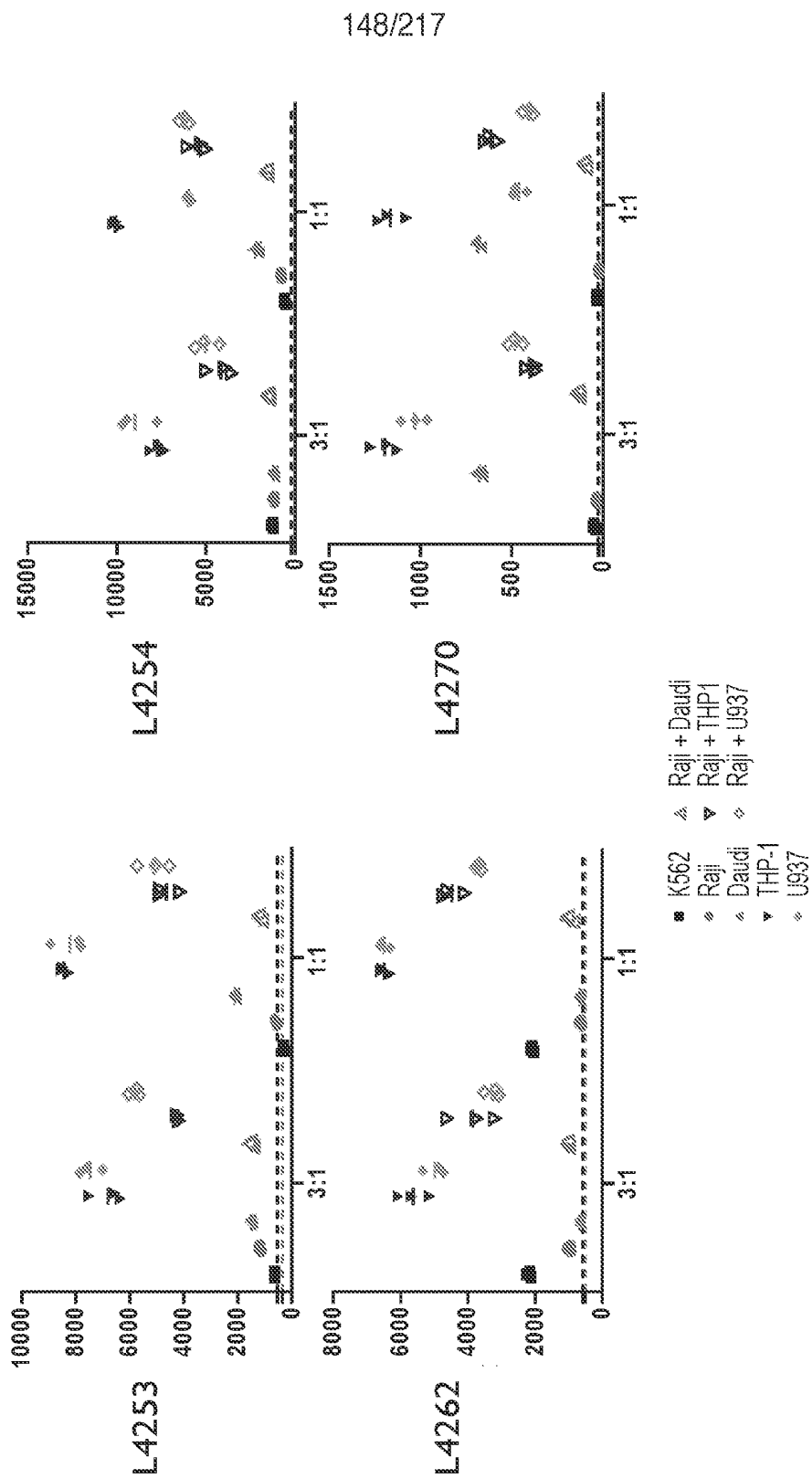


Figure 142

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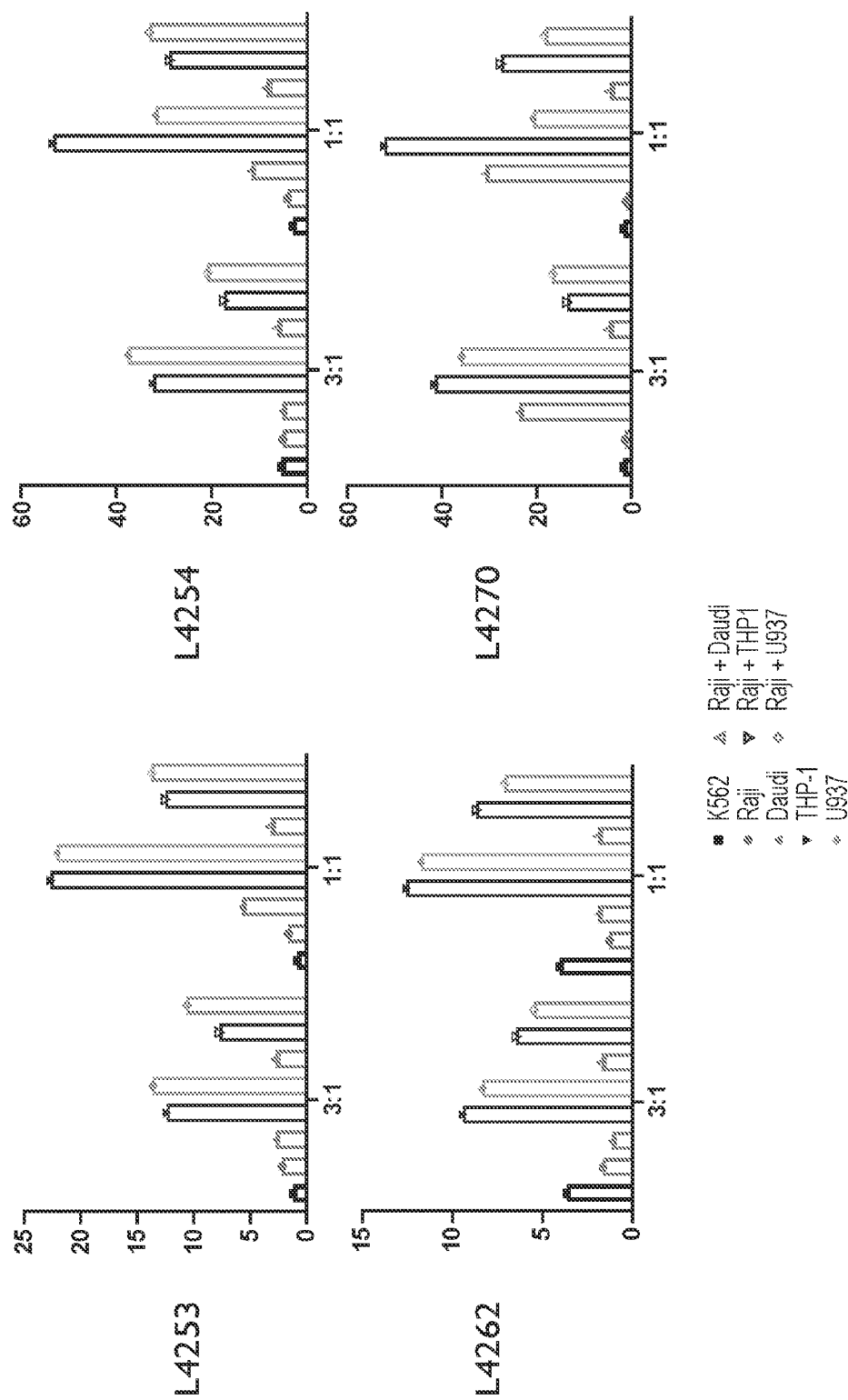


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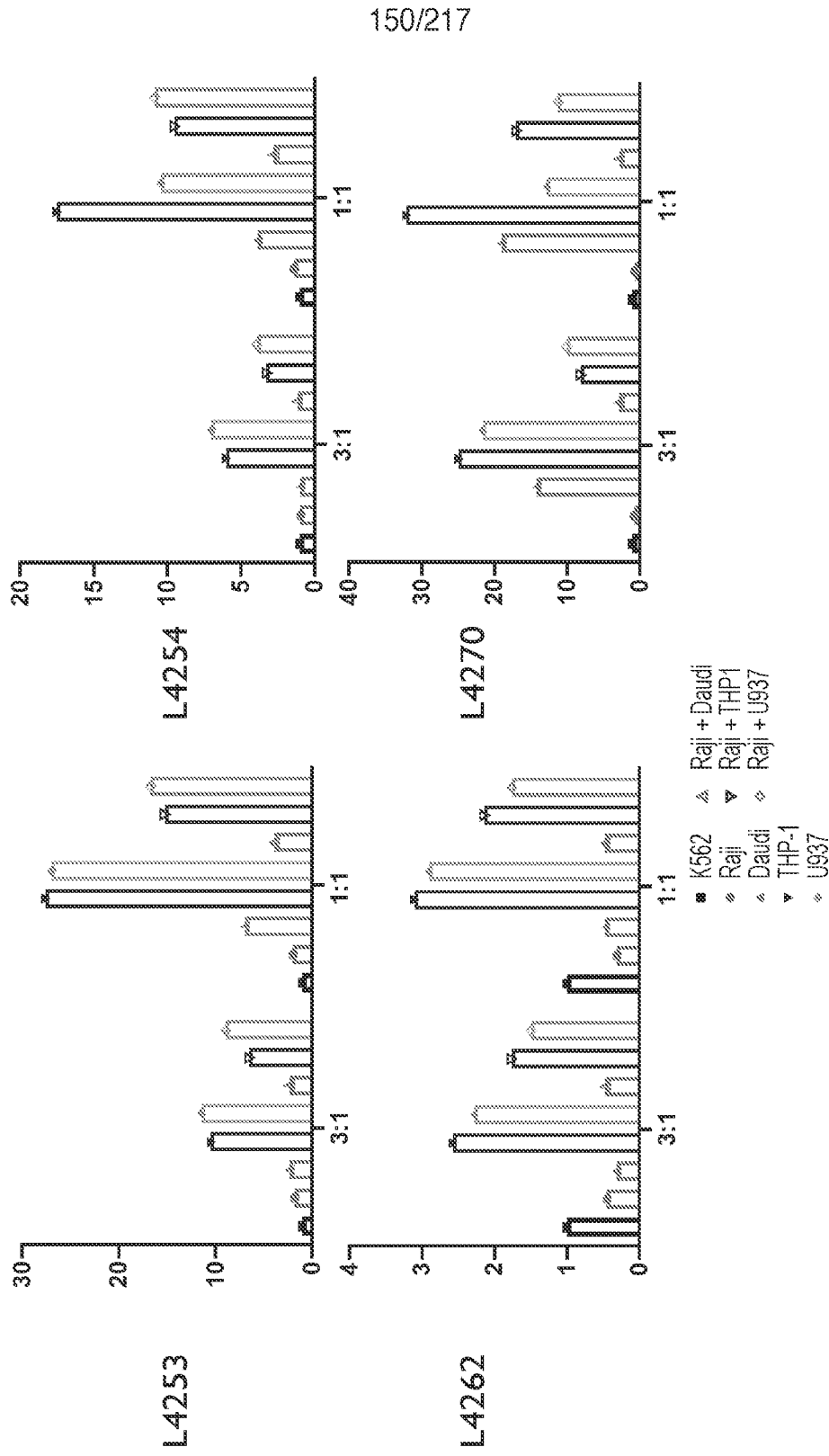


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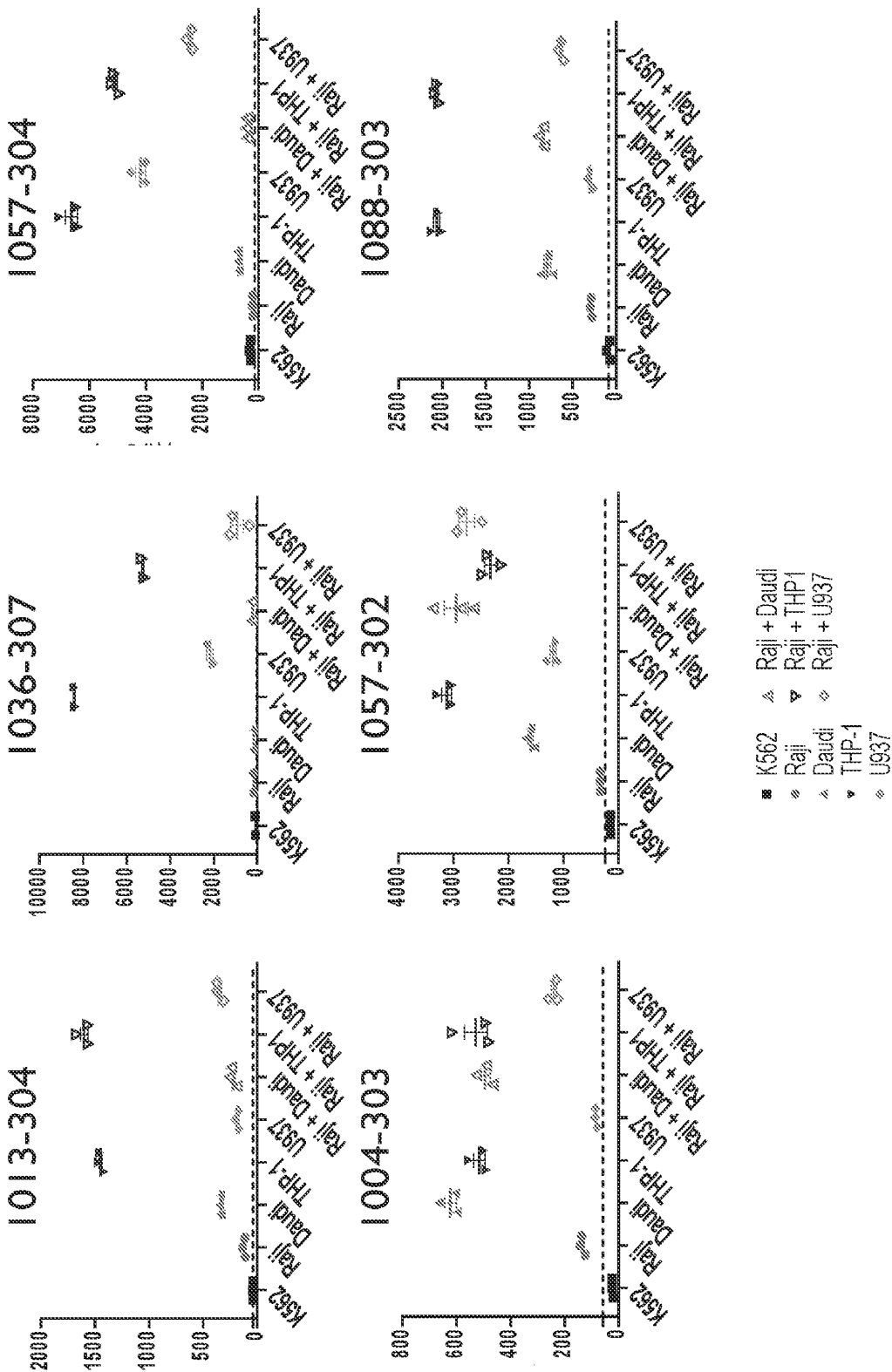


Figure 145

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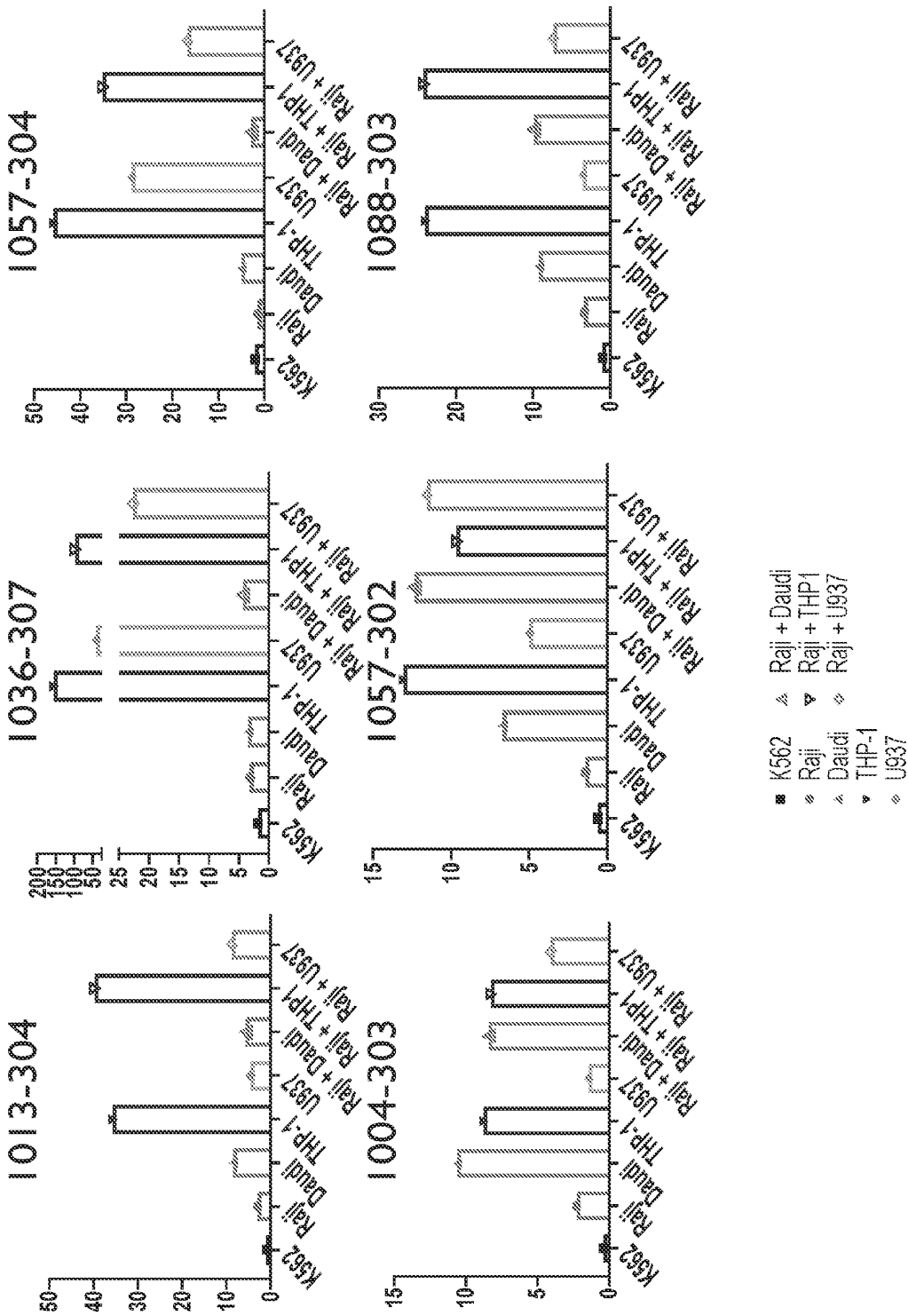


Figure 146

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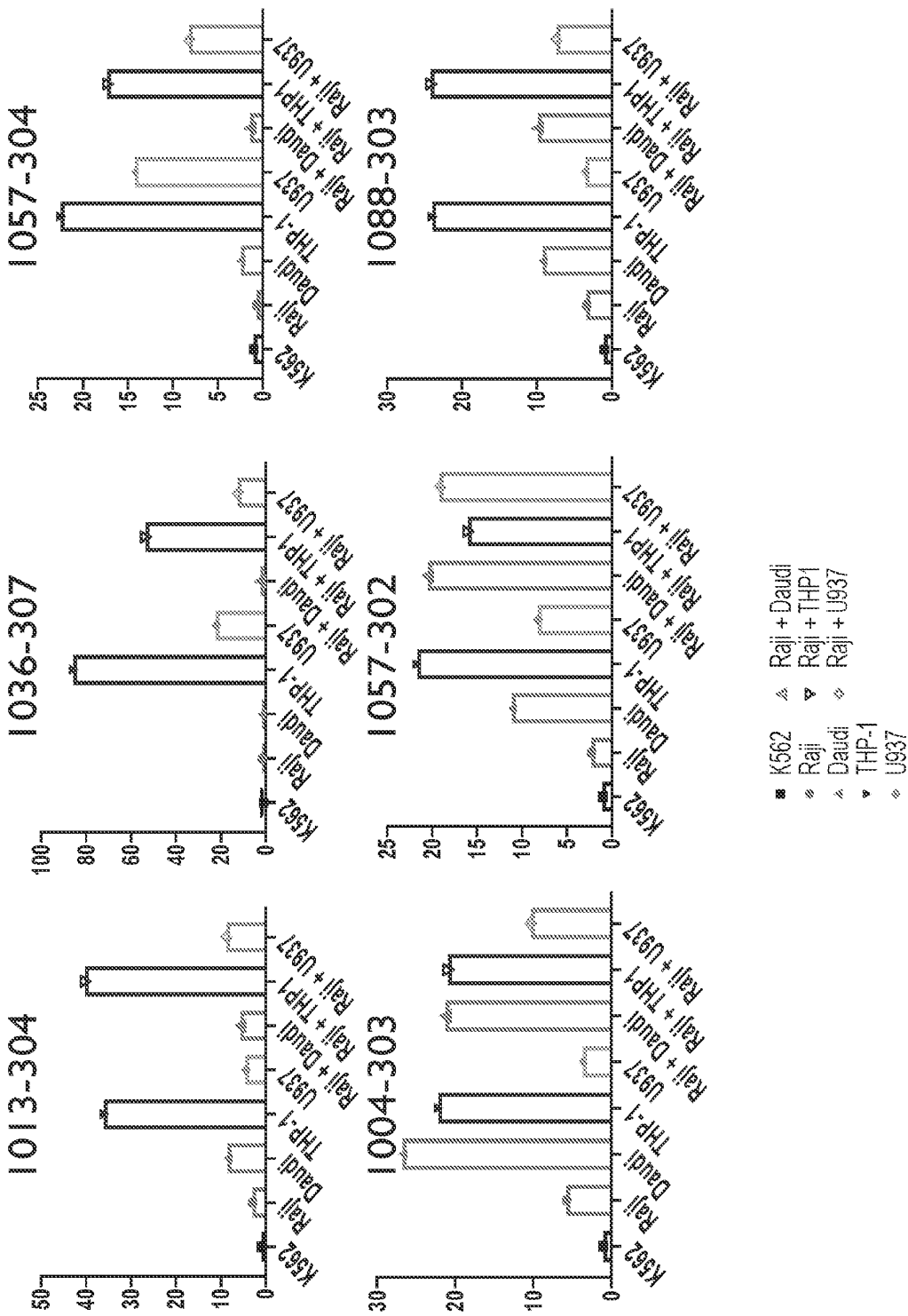


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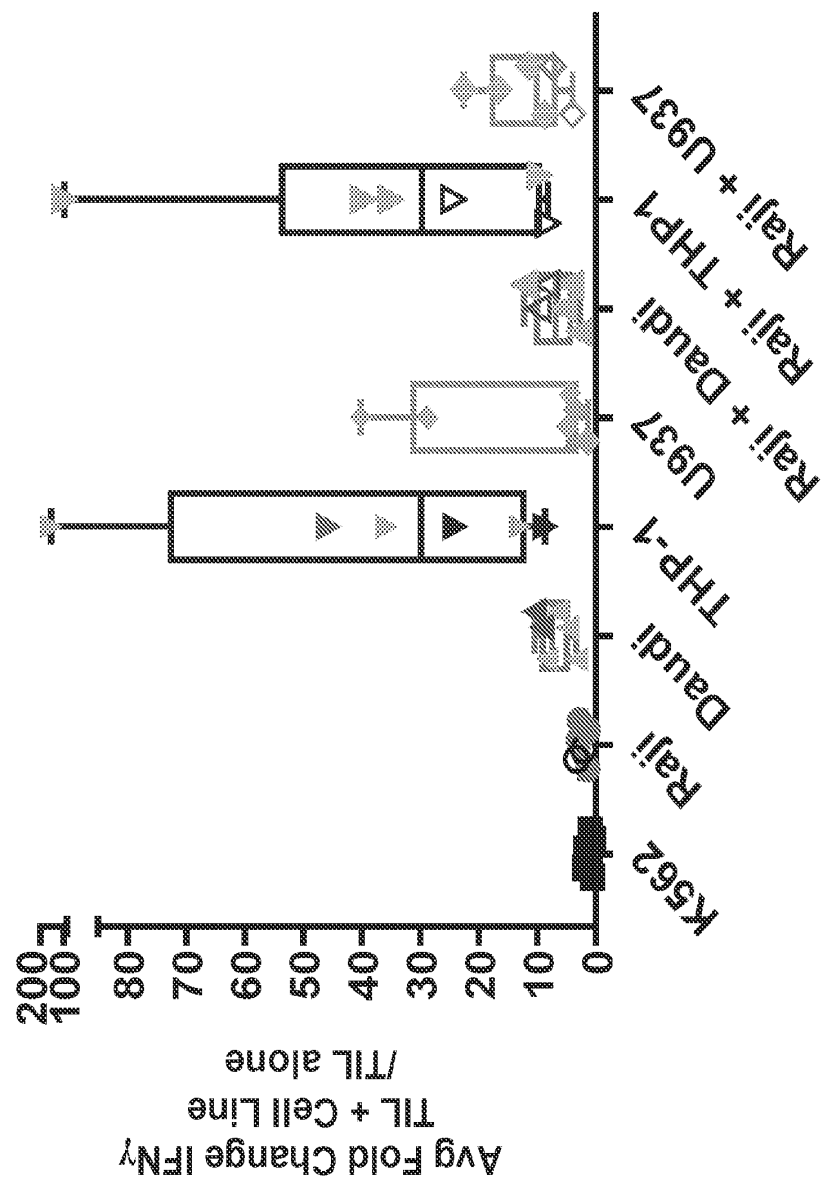


Figure 148

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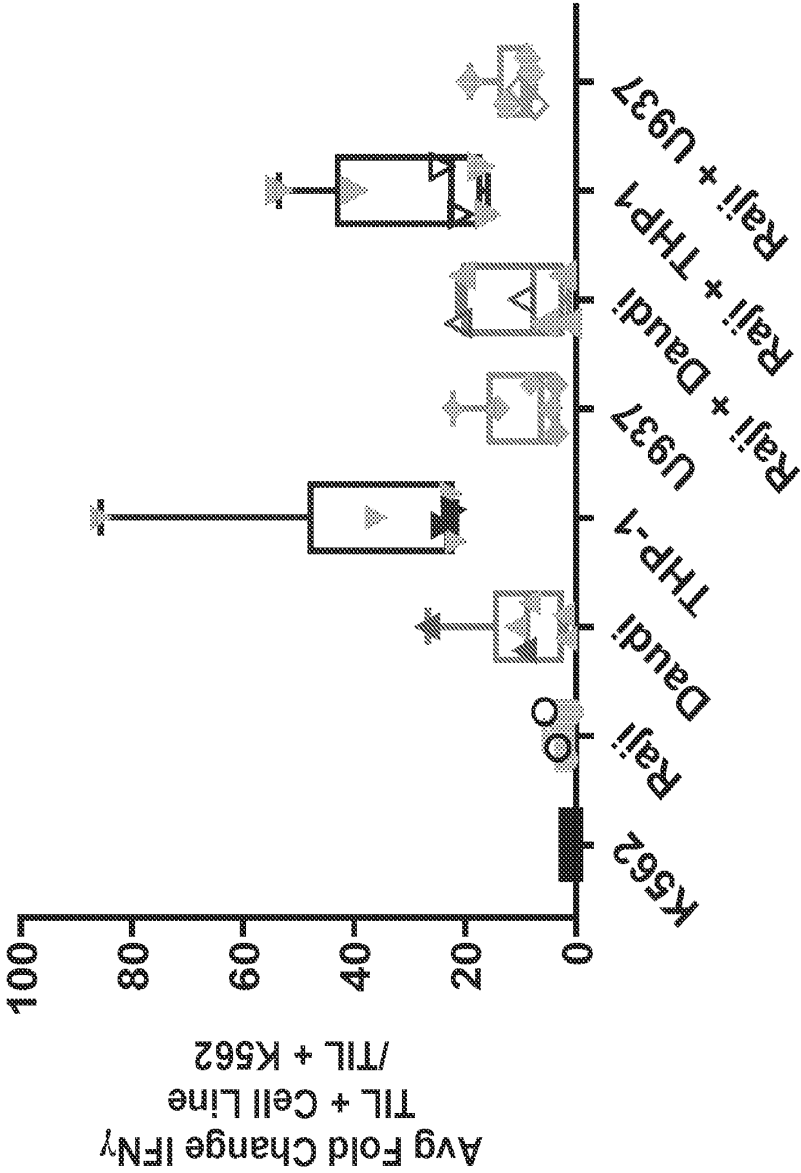


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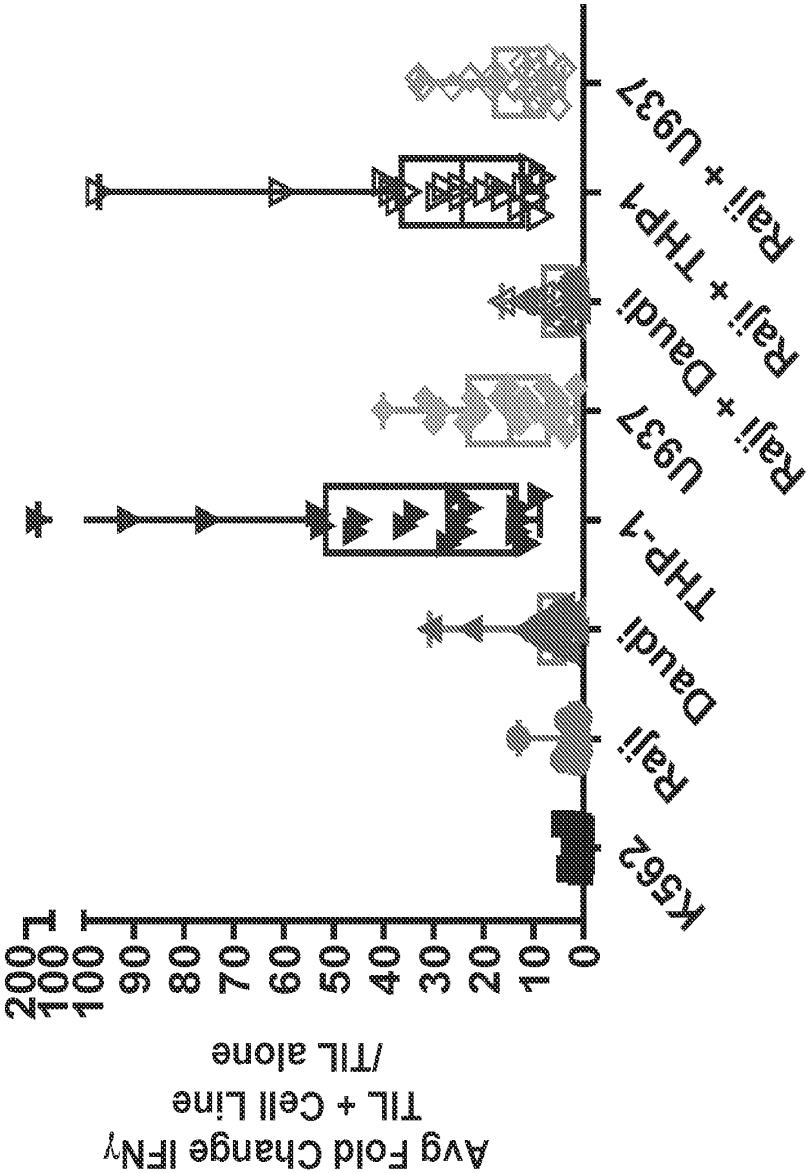


Figure 150

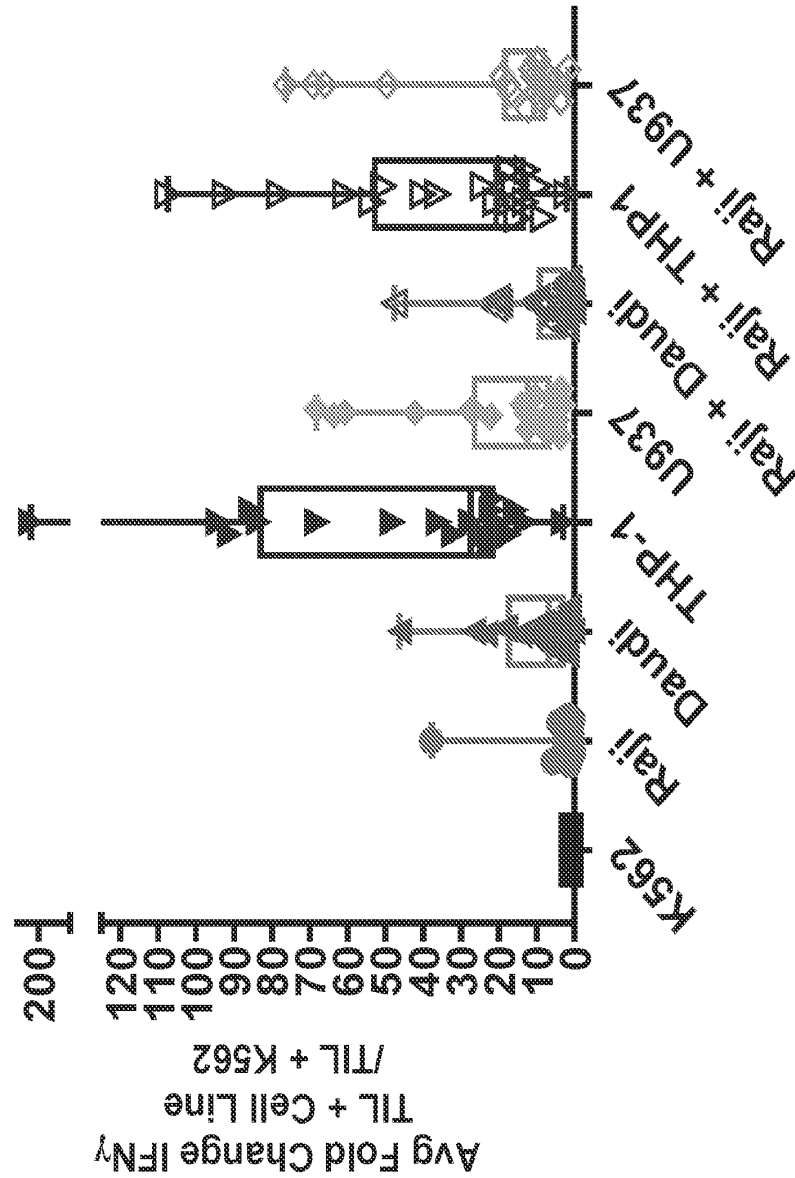


Figure 151

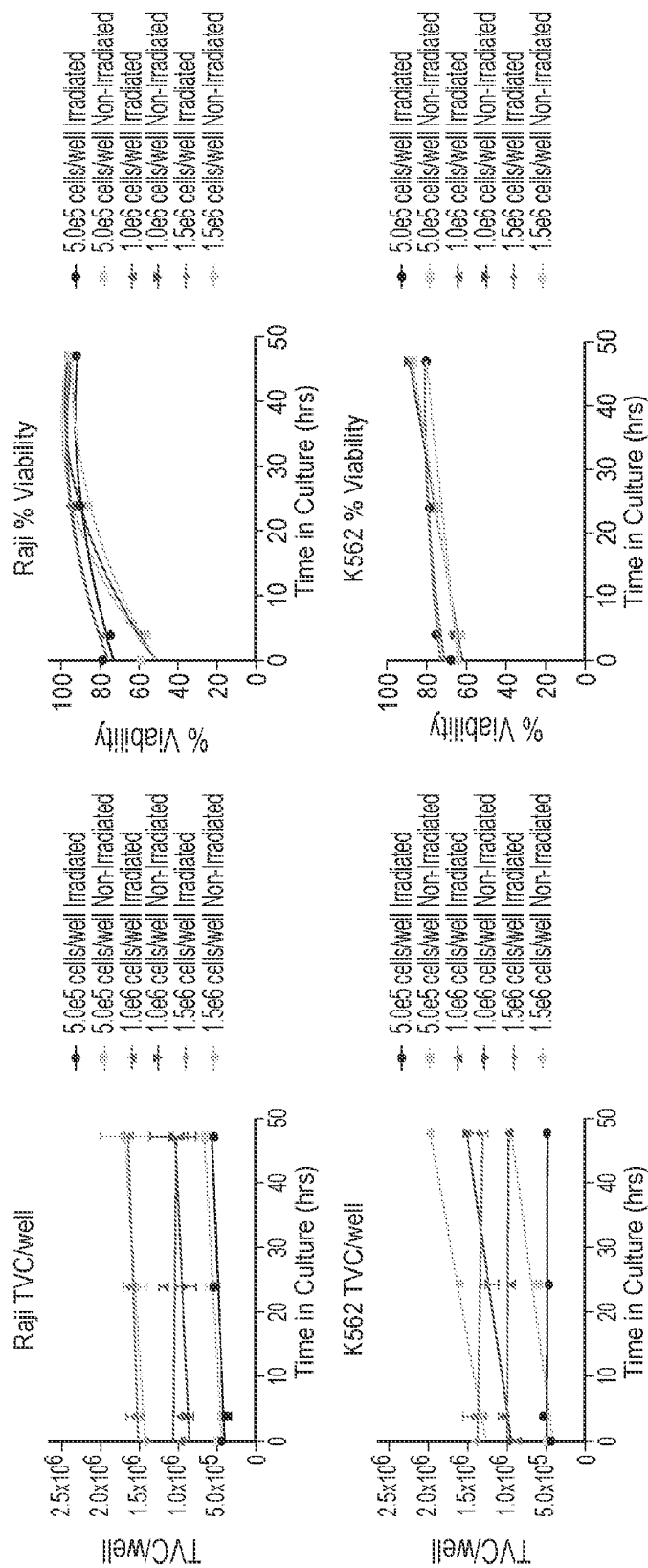


Figure 152

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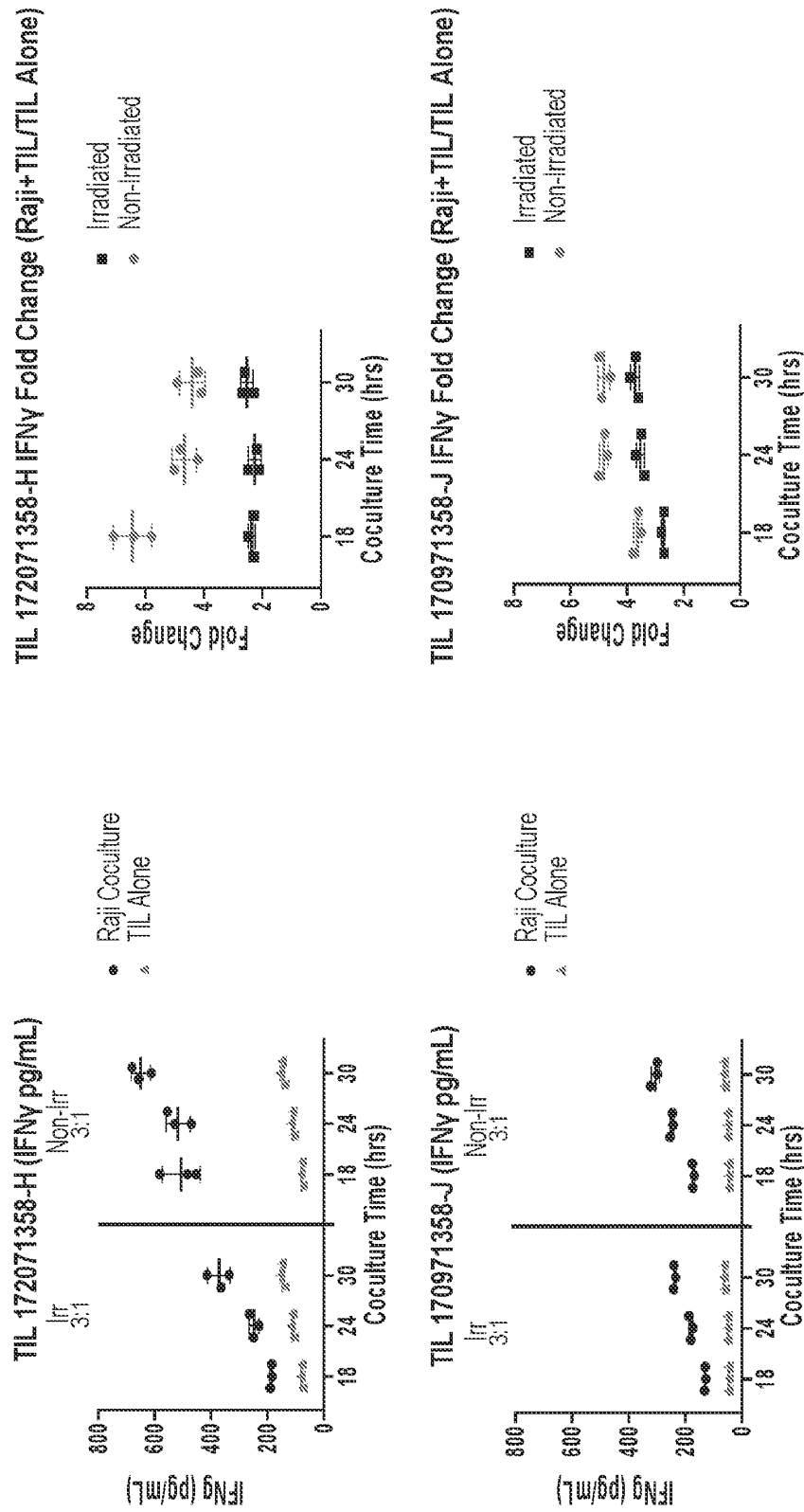


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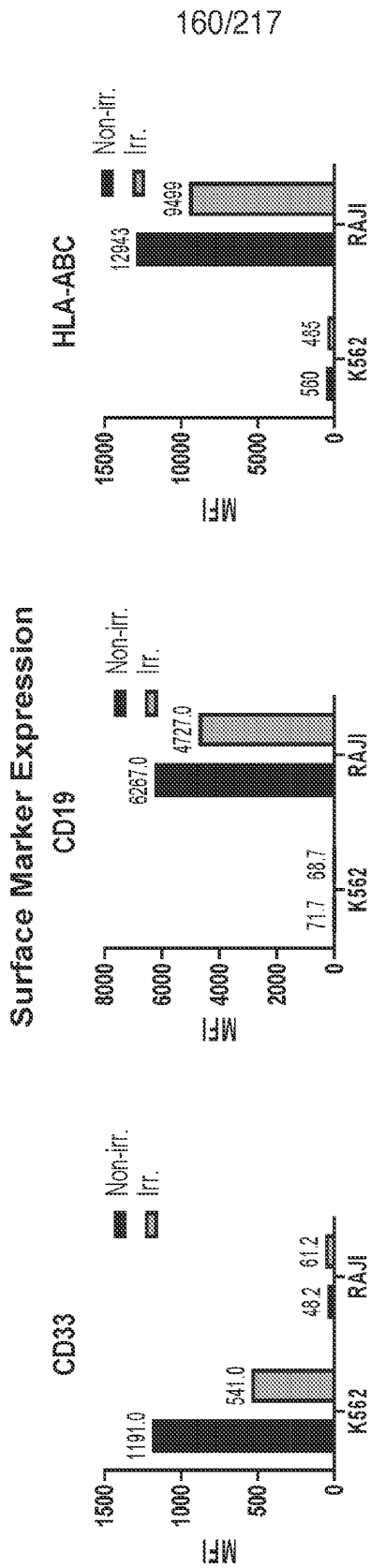


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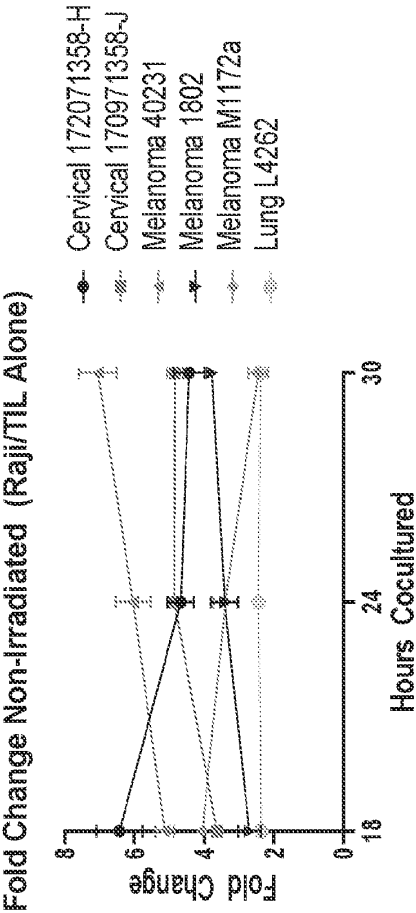


Figure 155

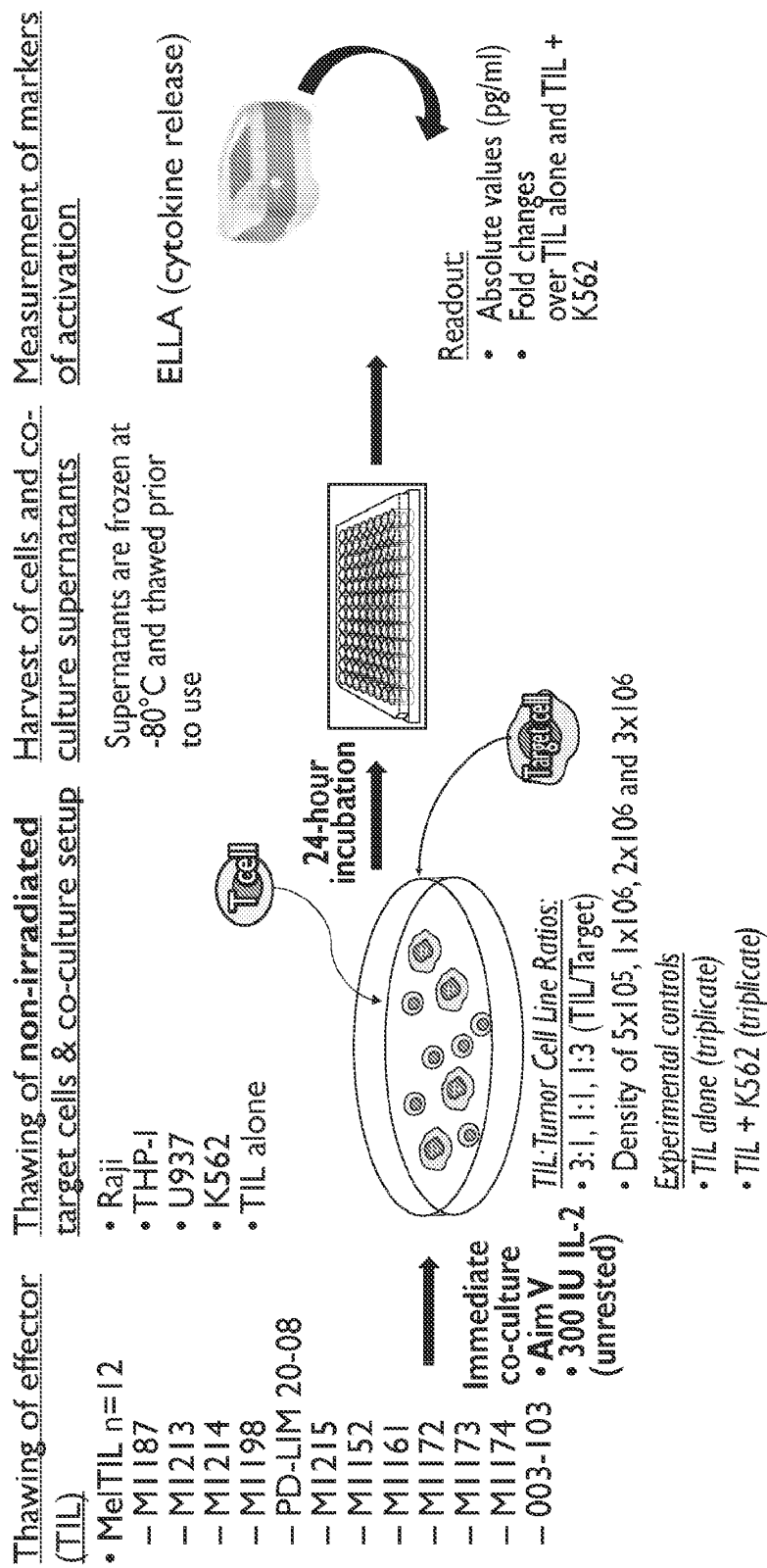


Figure 156

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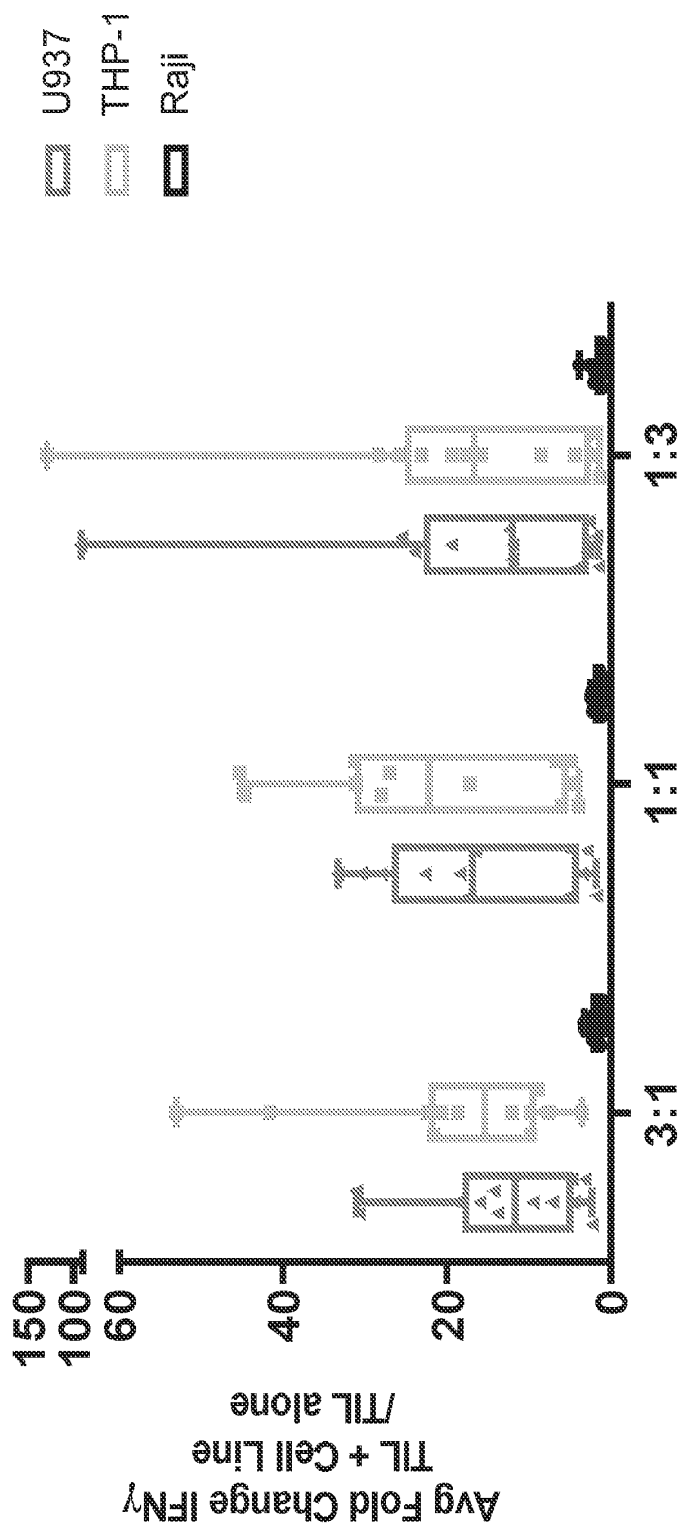


Figure 157

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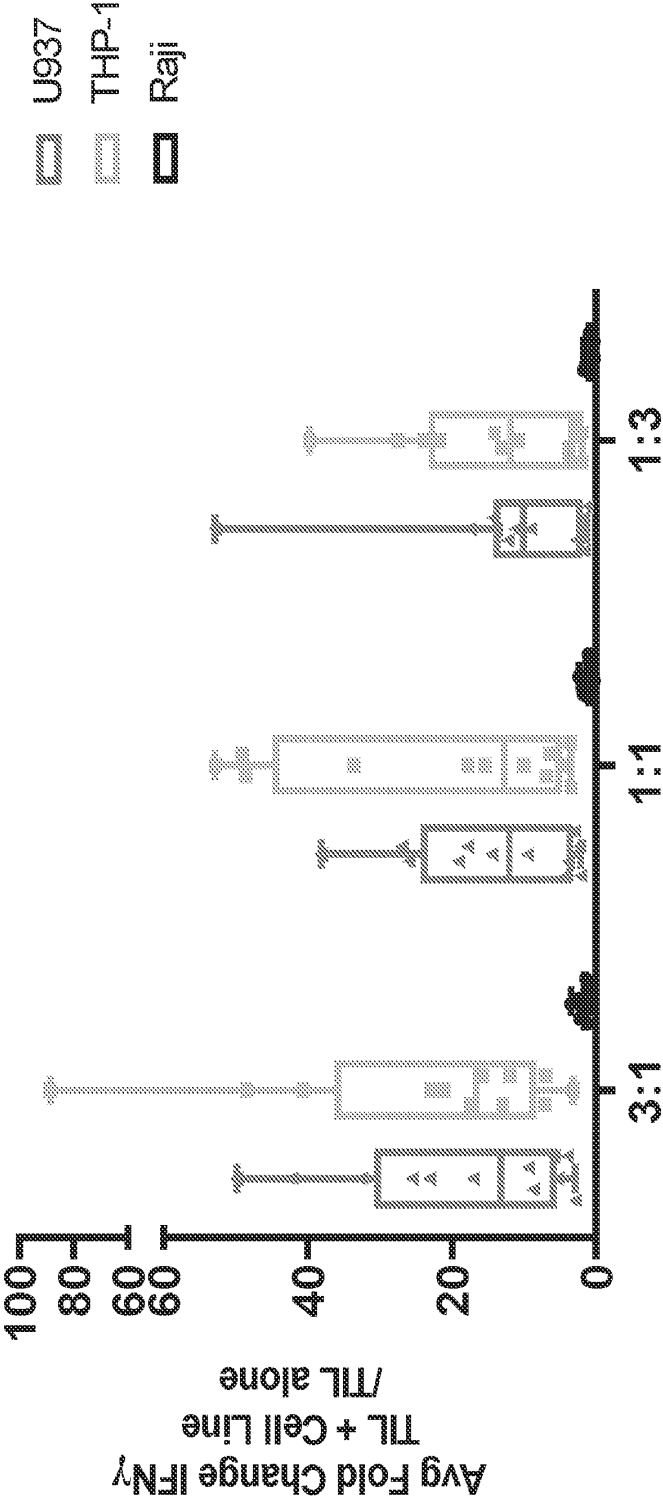


Figure 158

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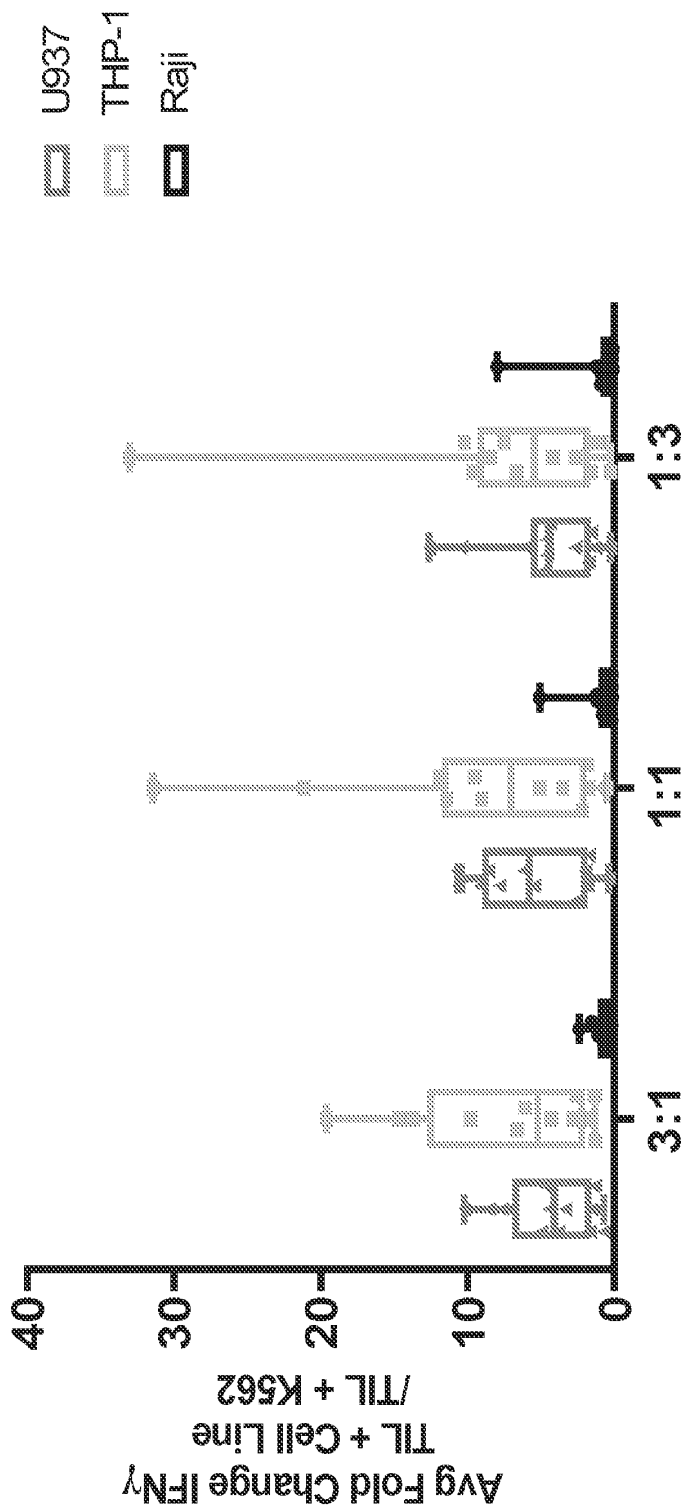


Figure 159

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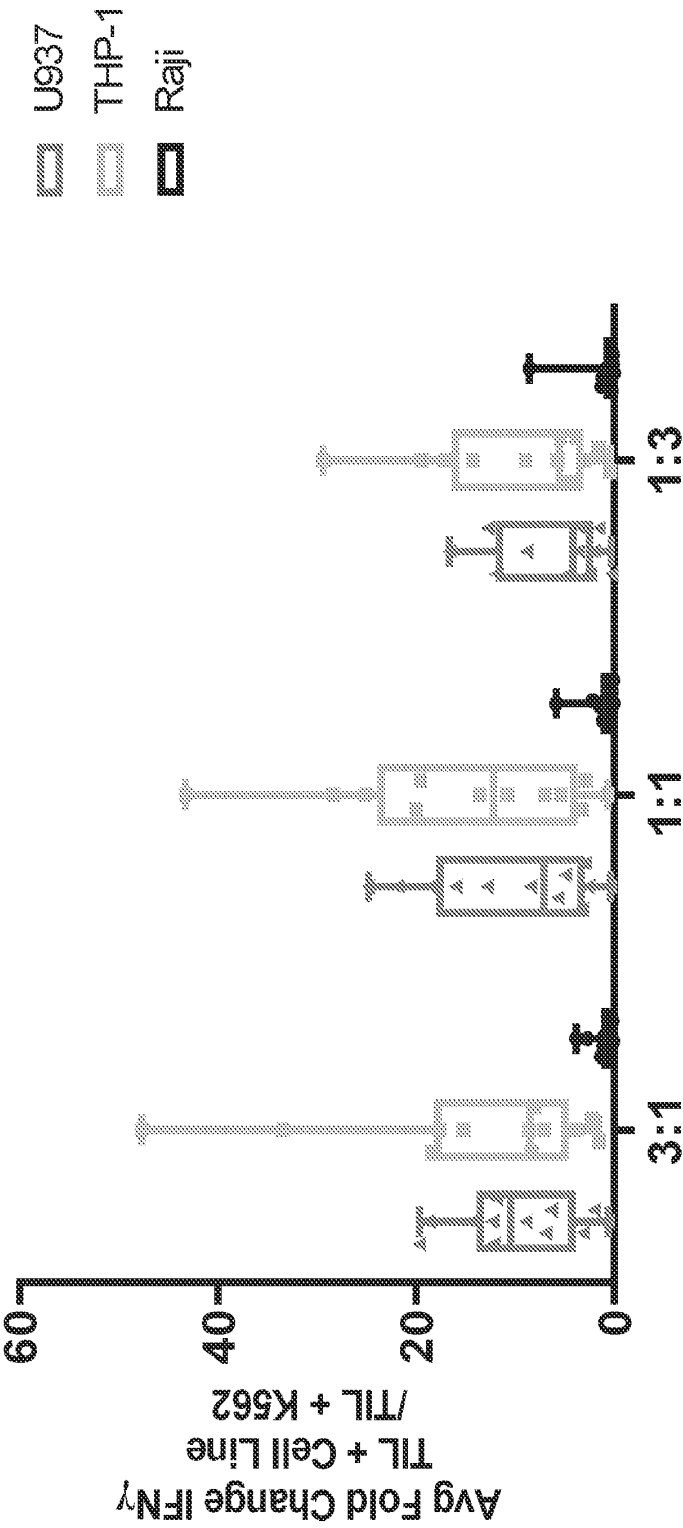


Figure 160

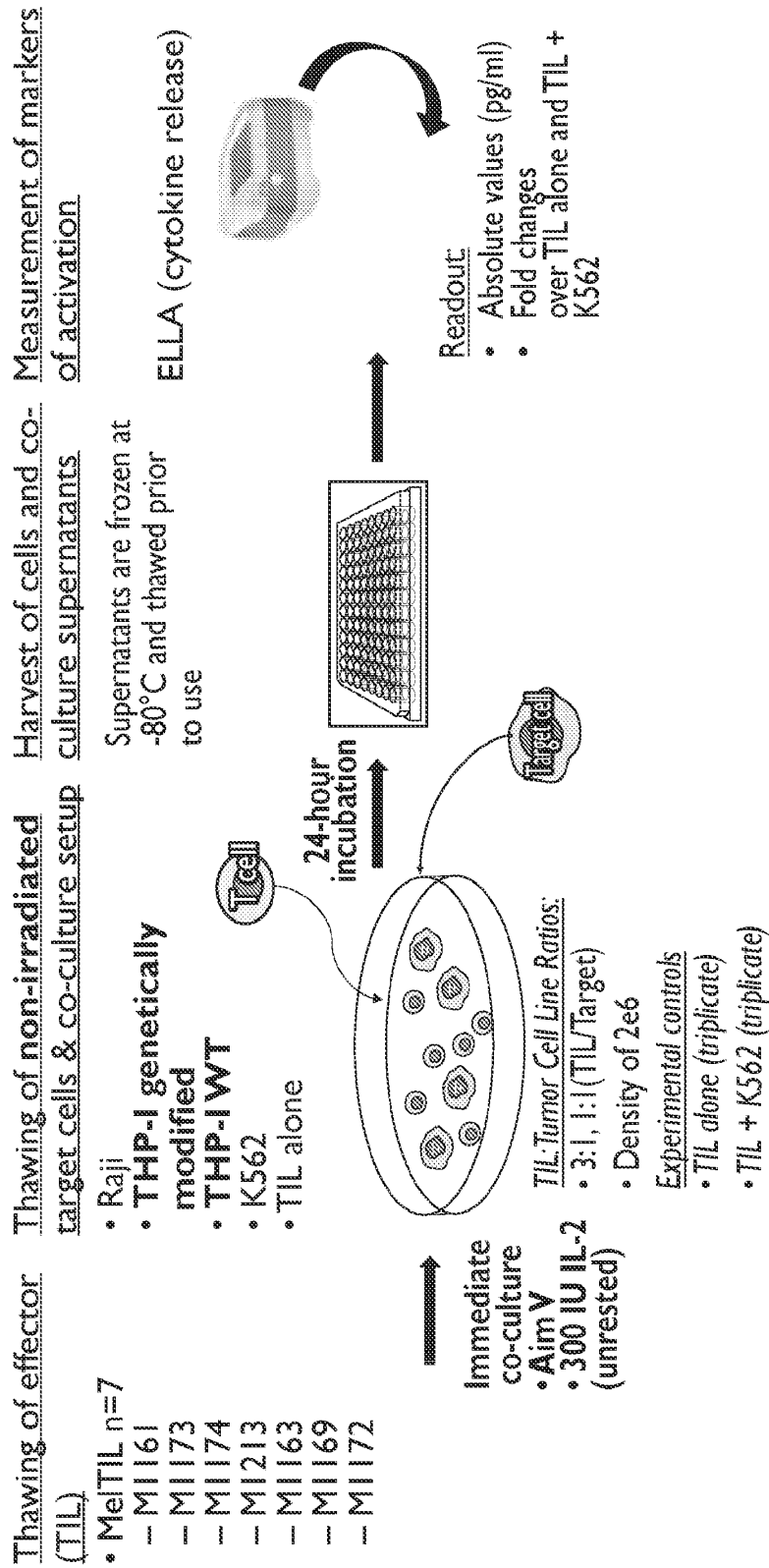


Figure 161

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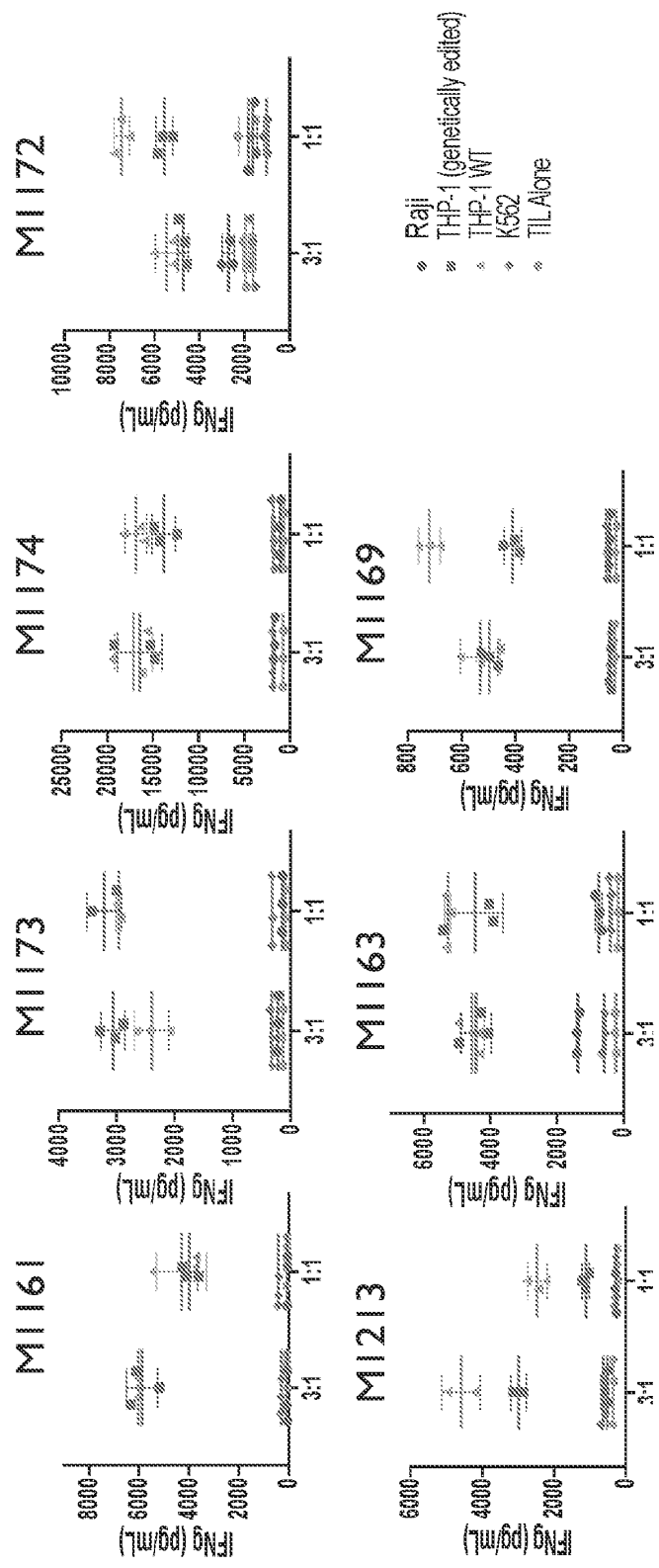


Figure 162

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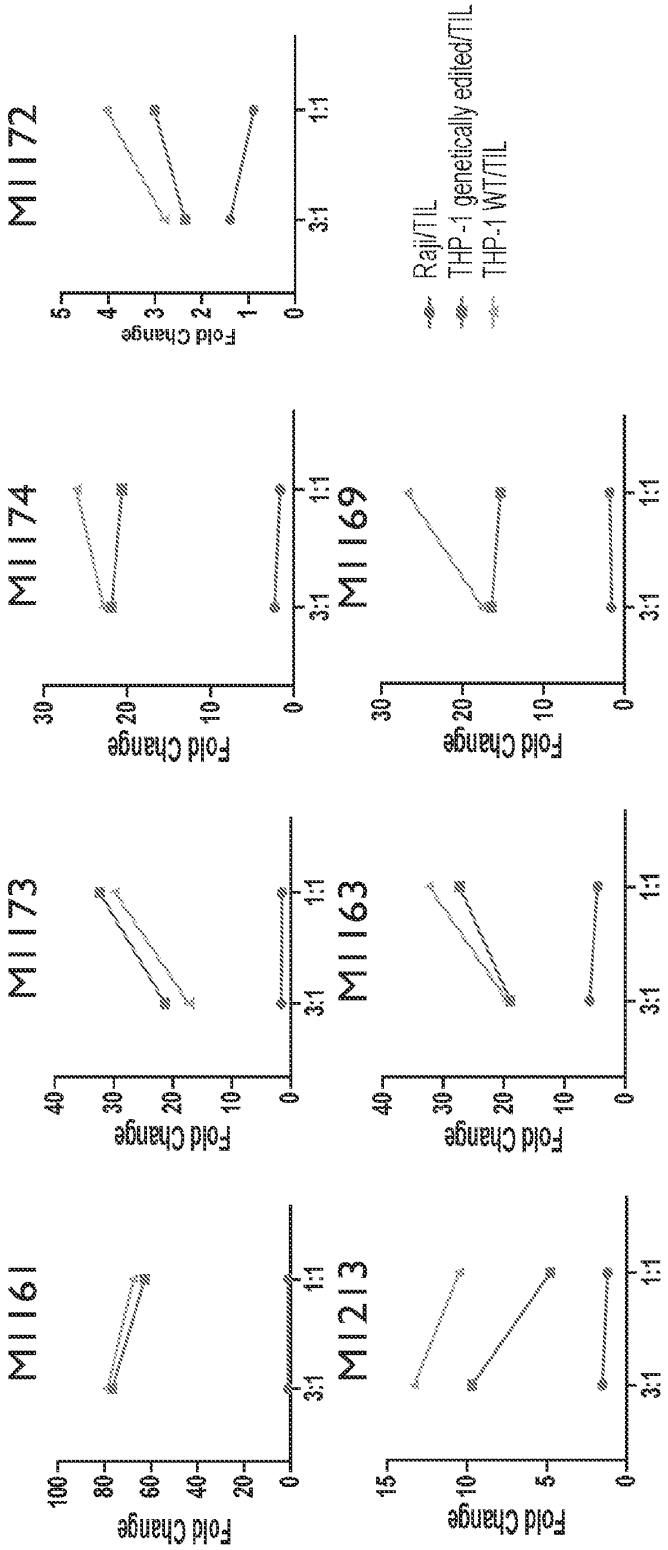


Figure 163

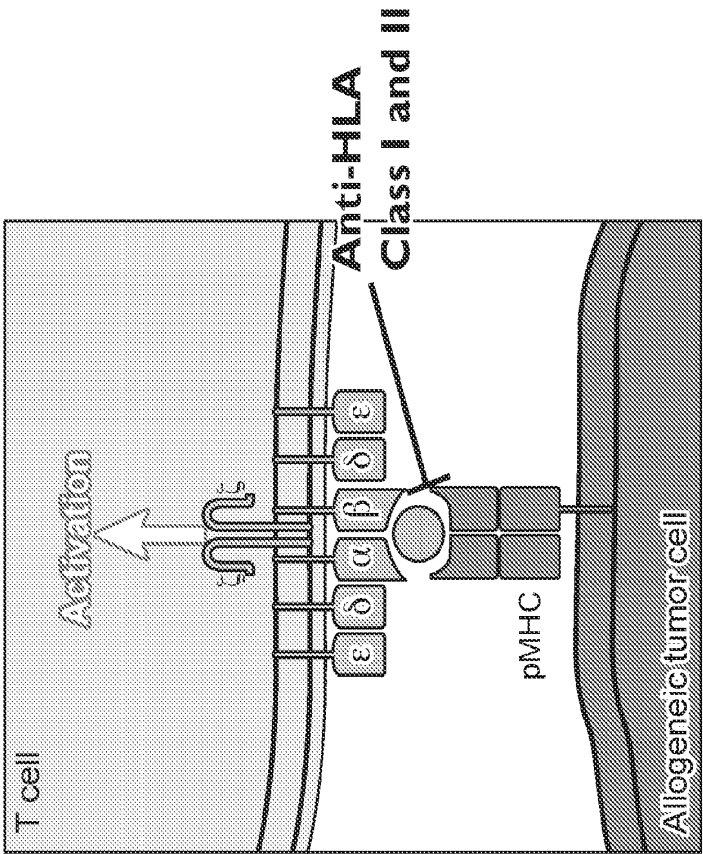


Figure 164

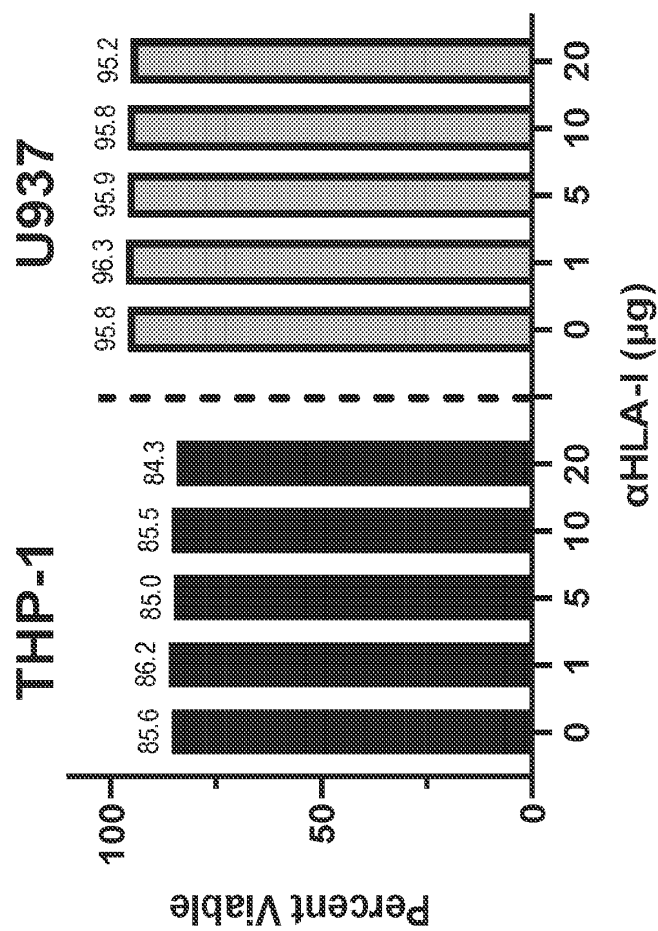


Figure 165

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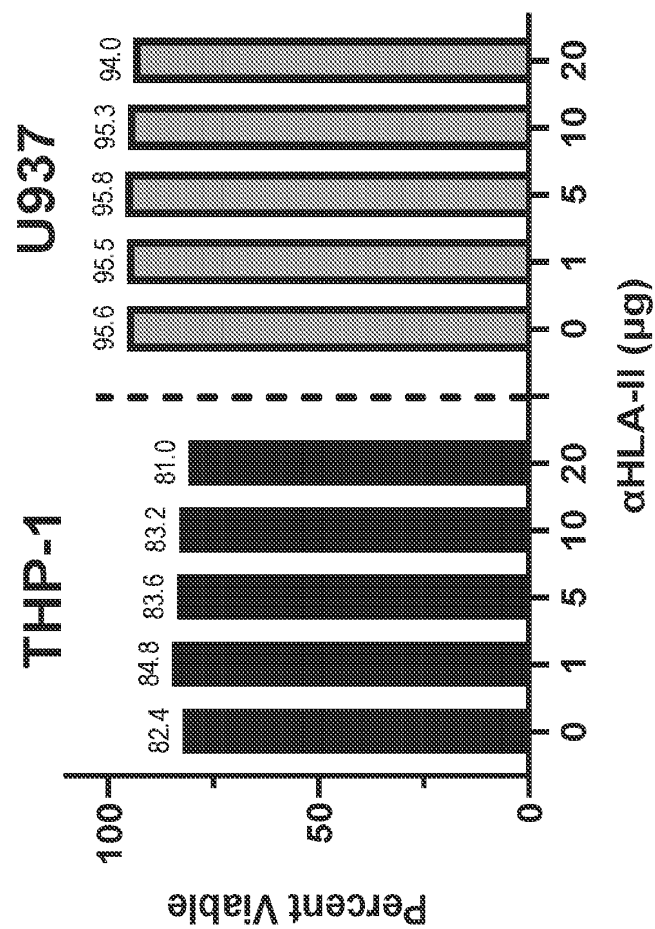


Figure 166

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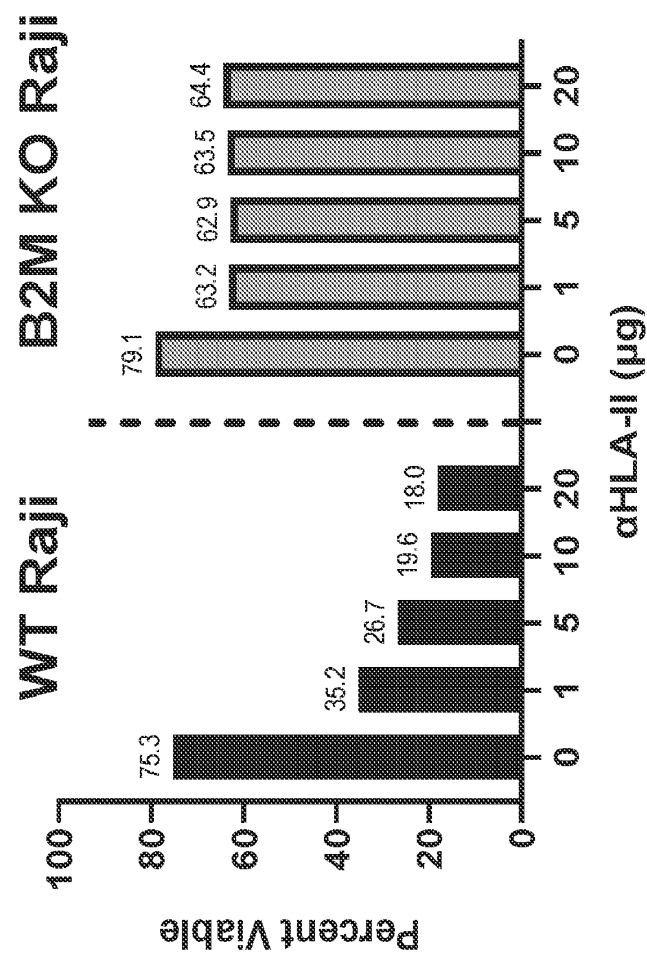


Figure 167

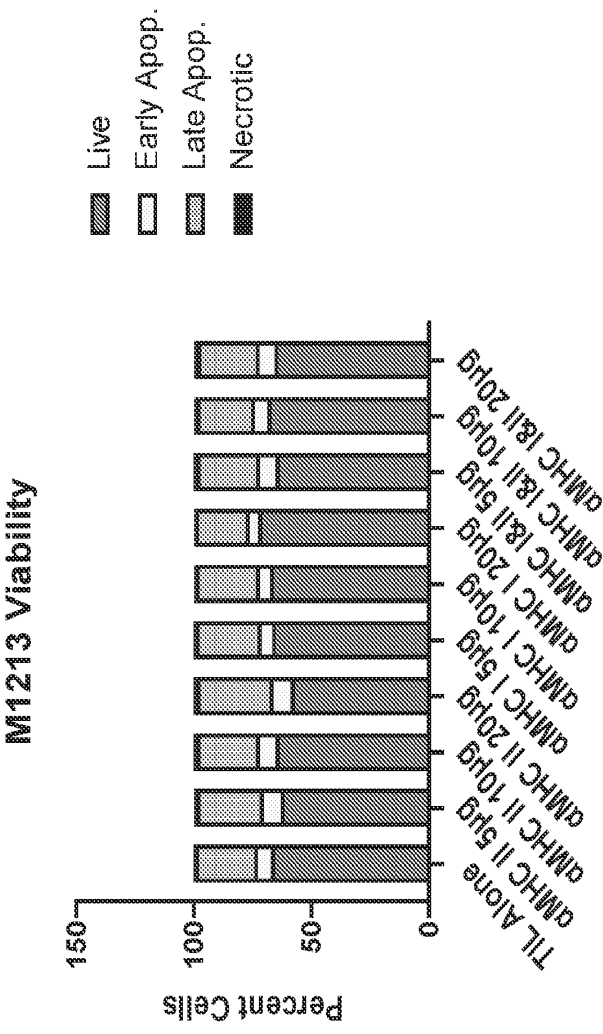


Figure 168

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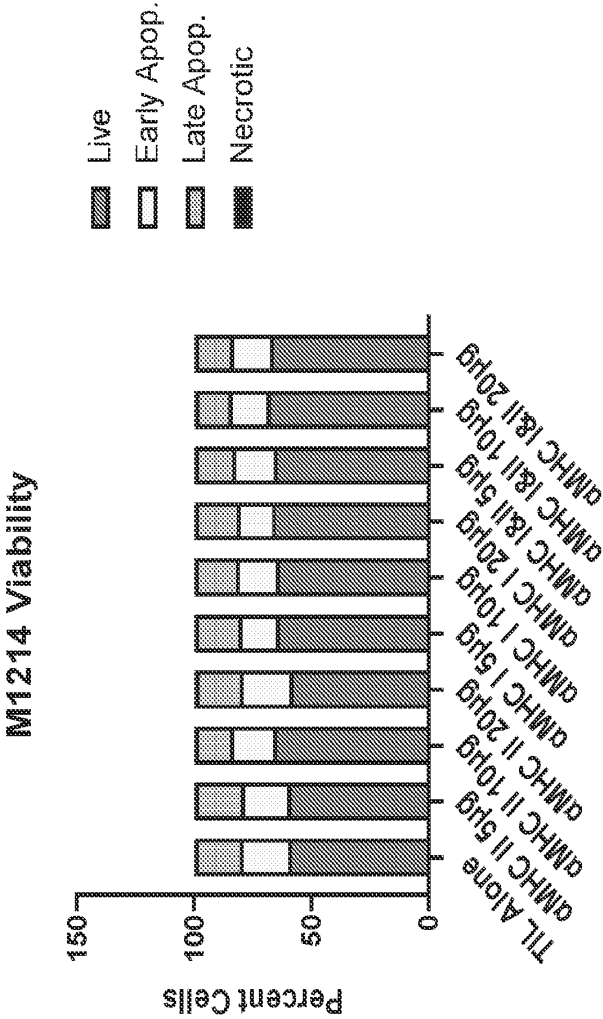


Figure 169

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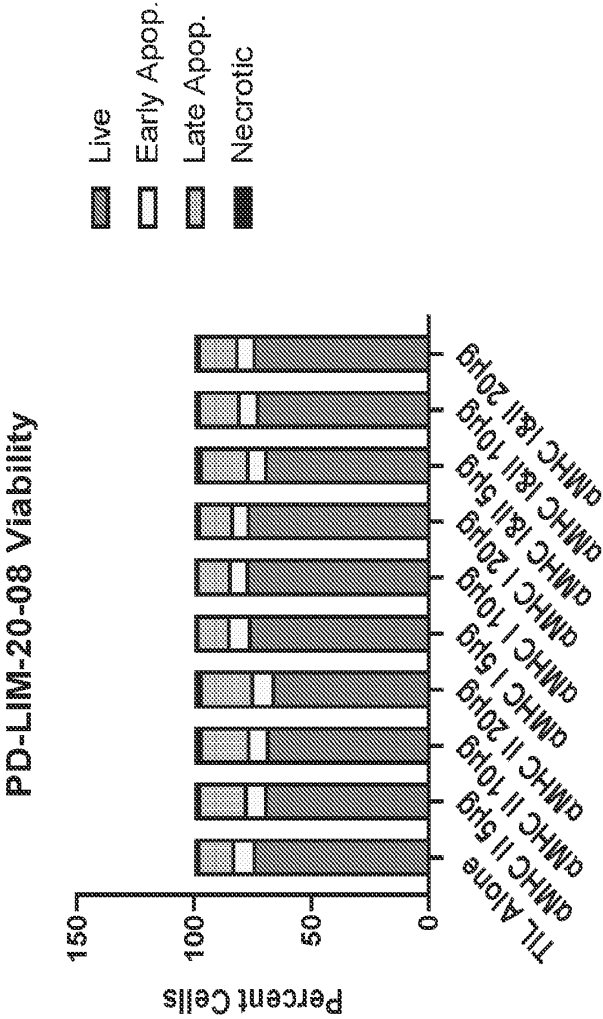


Figure 170

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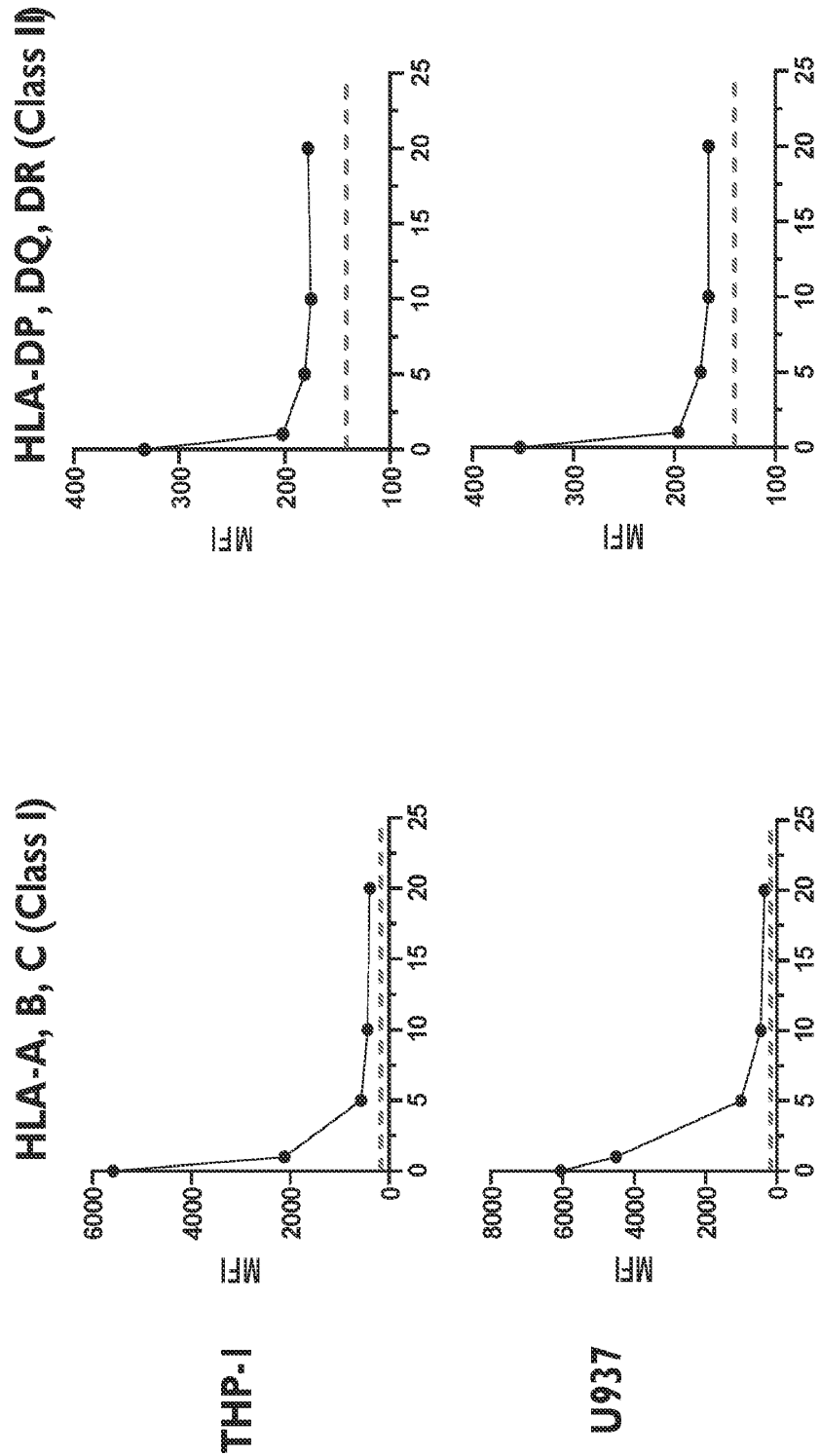


Figure 171

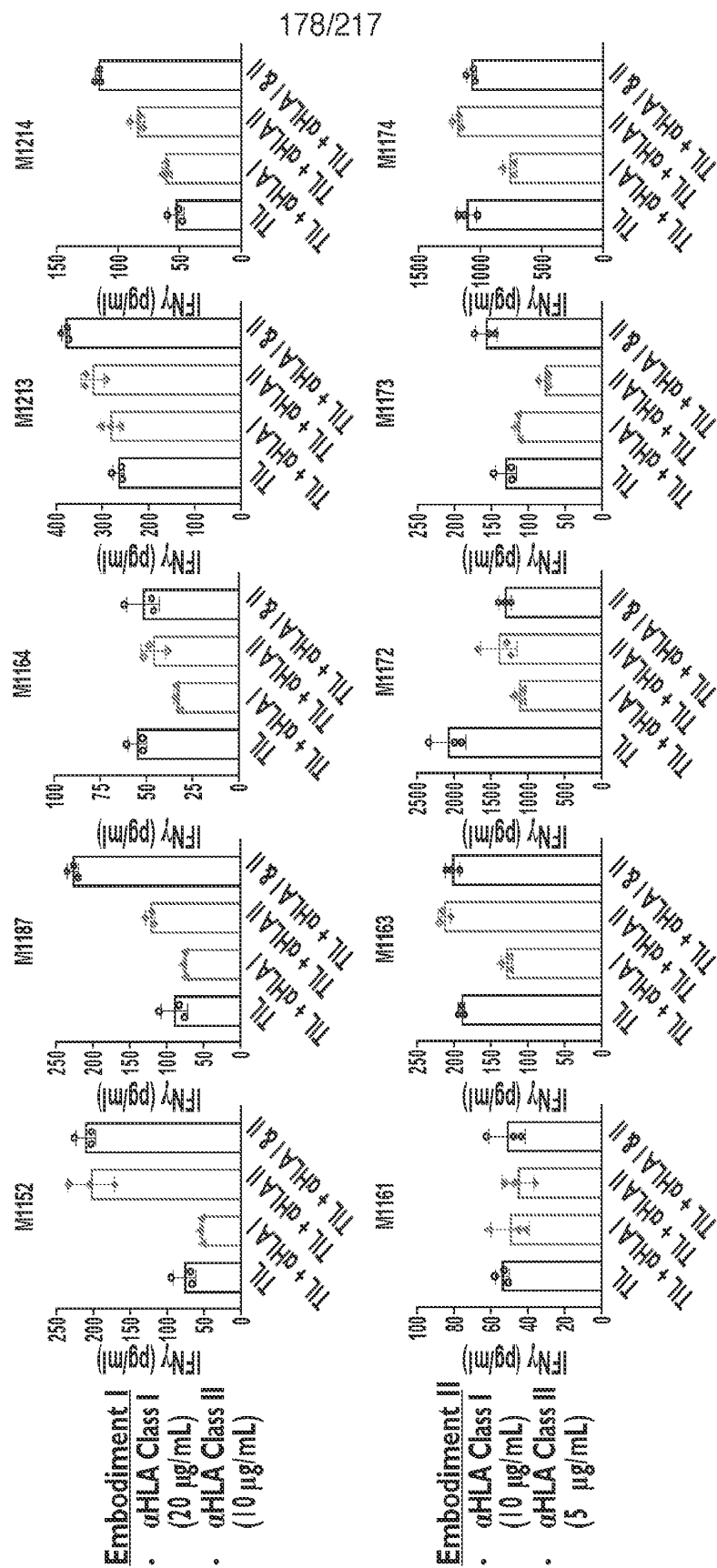


Figure 172

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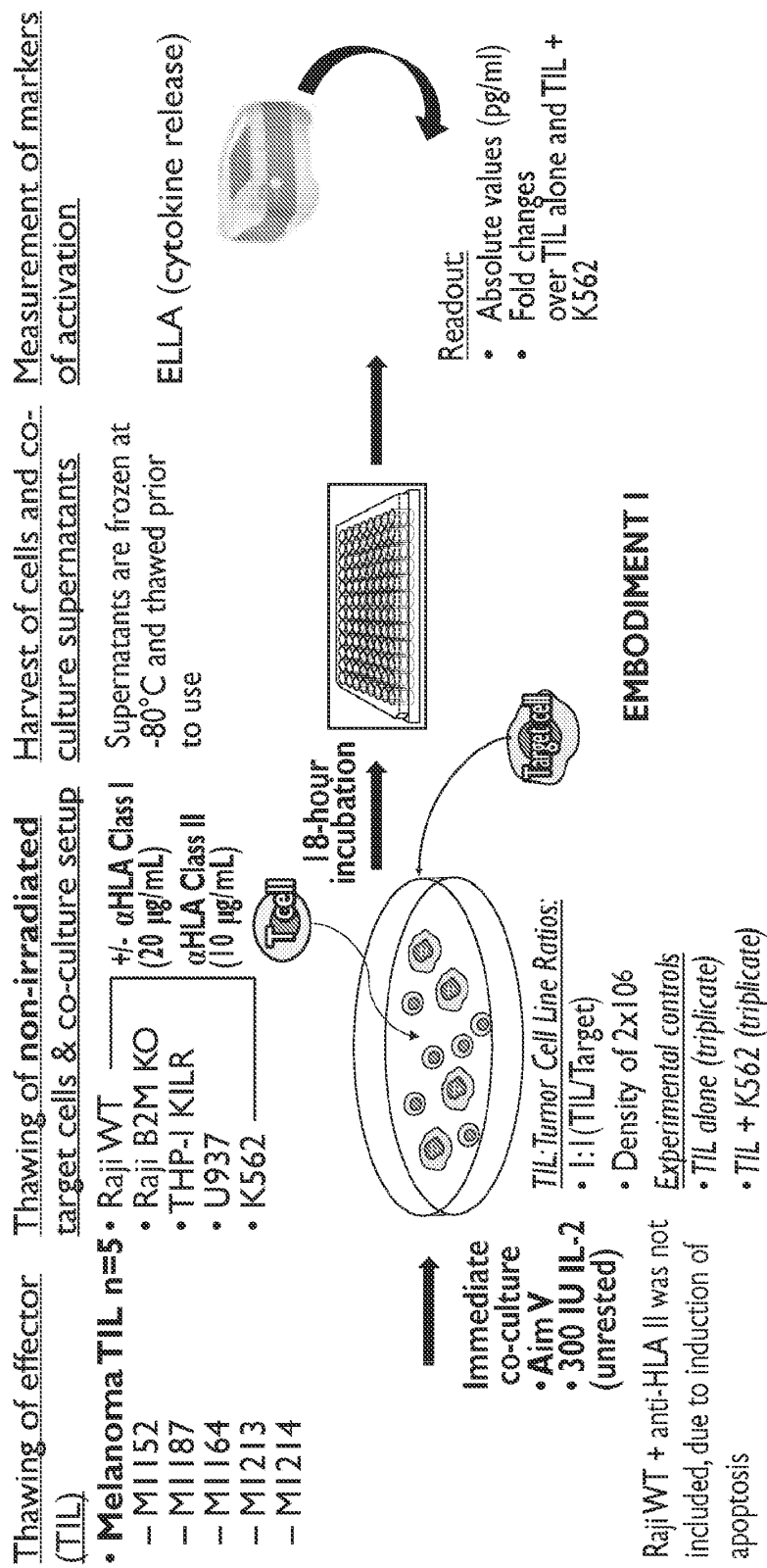


Figure 173

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M1152

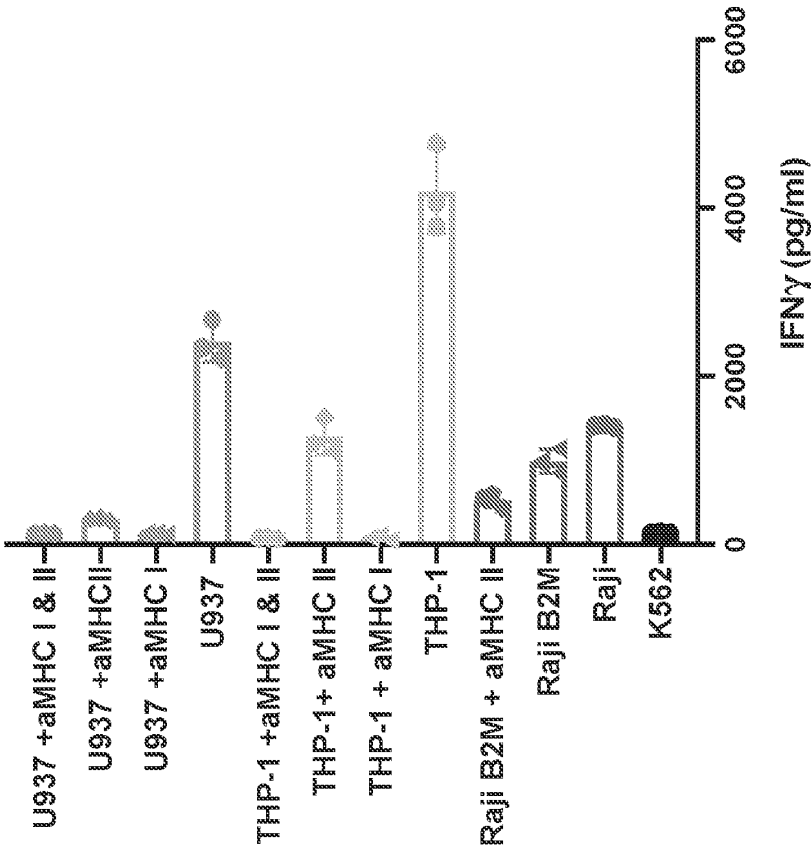


Figure 174

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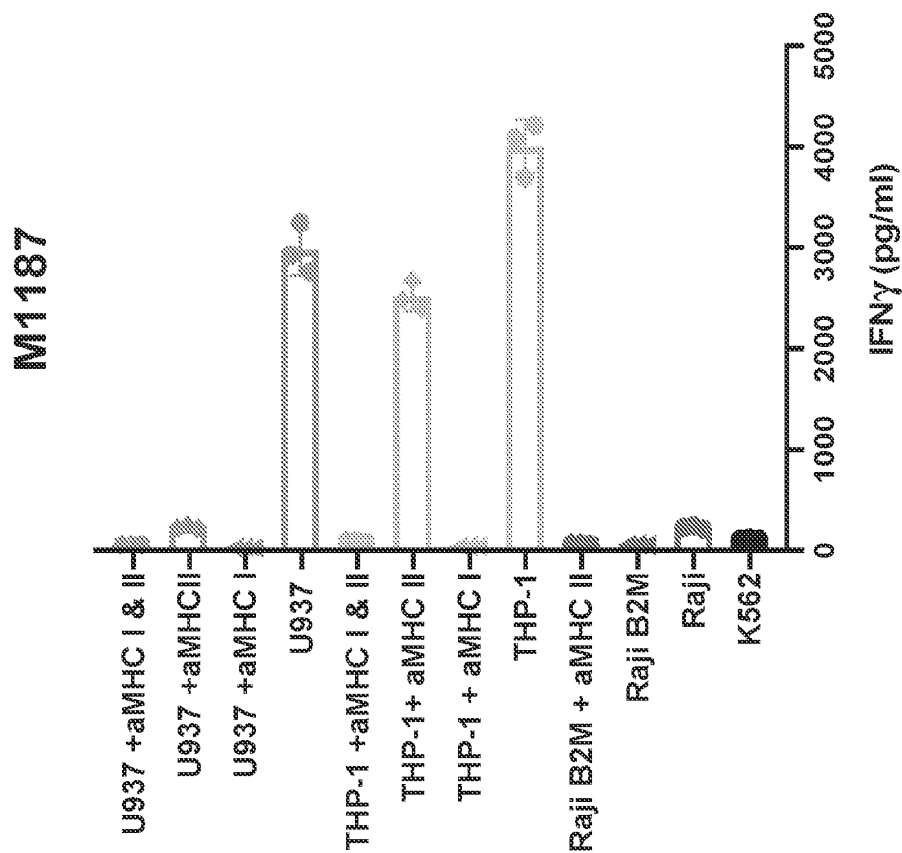


Figure 175

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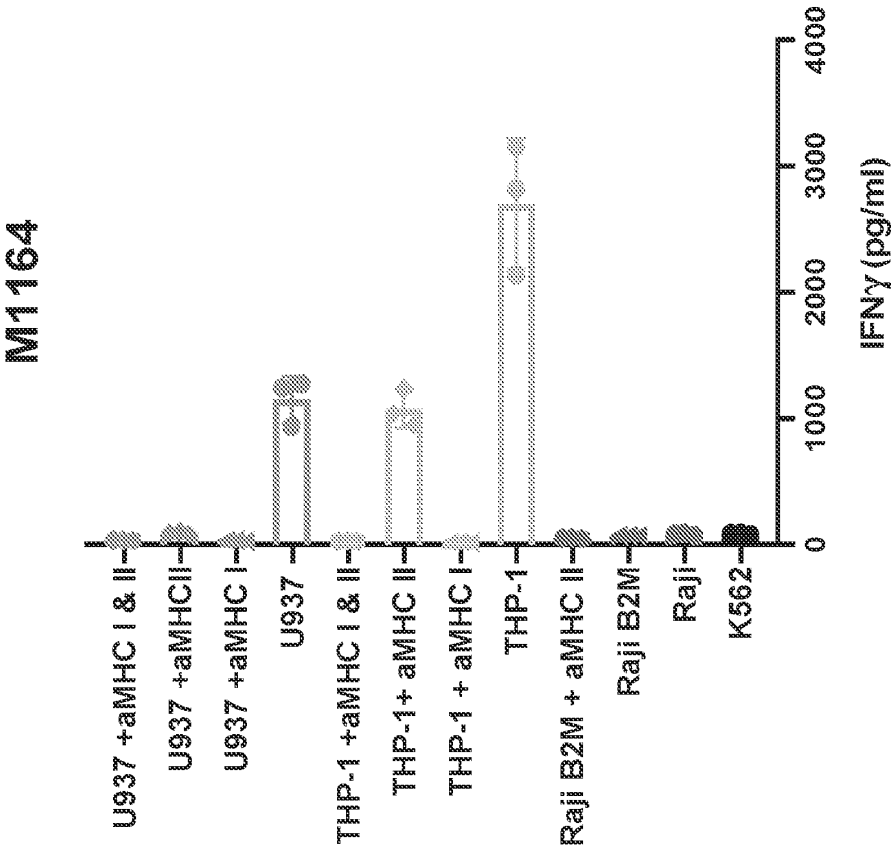


Figure 176

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M1213

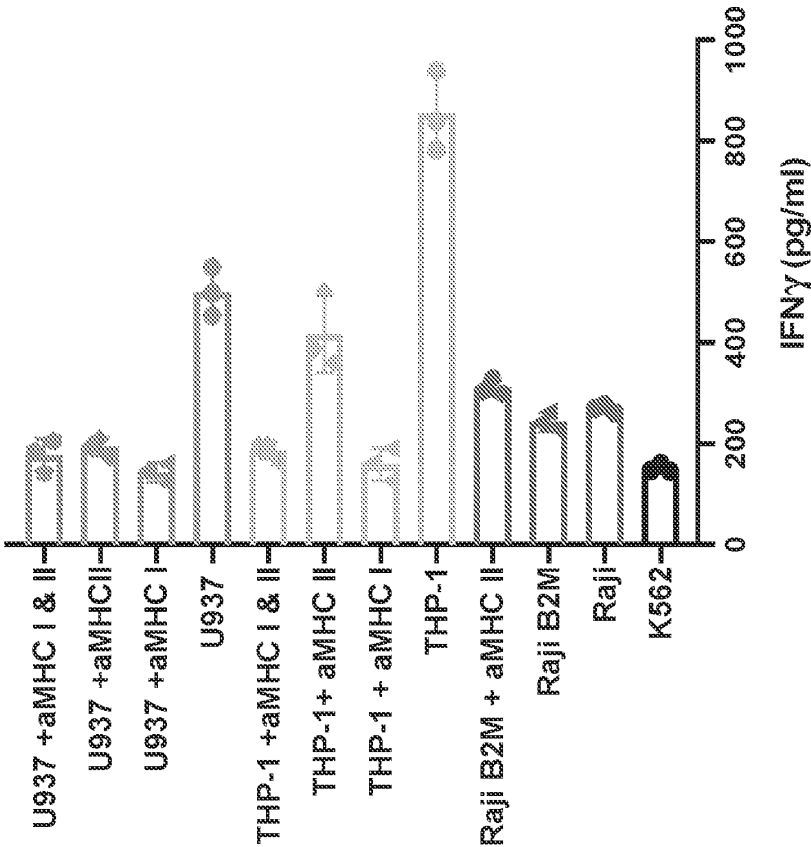


Figure 177

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M1214

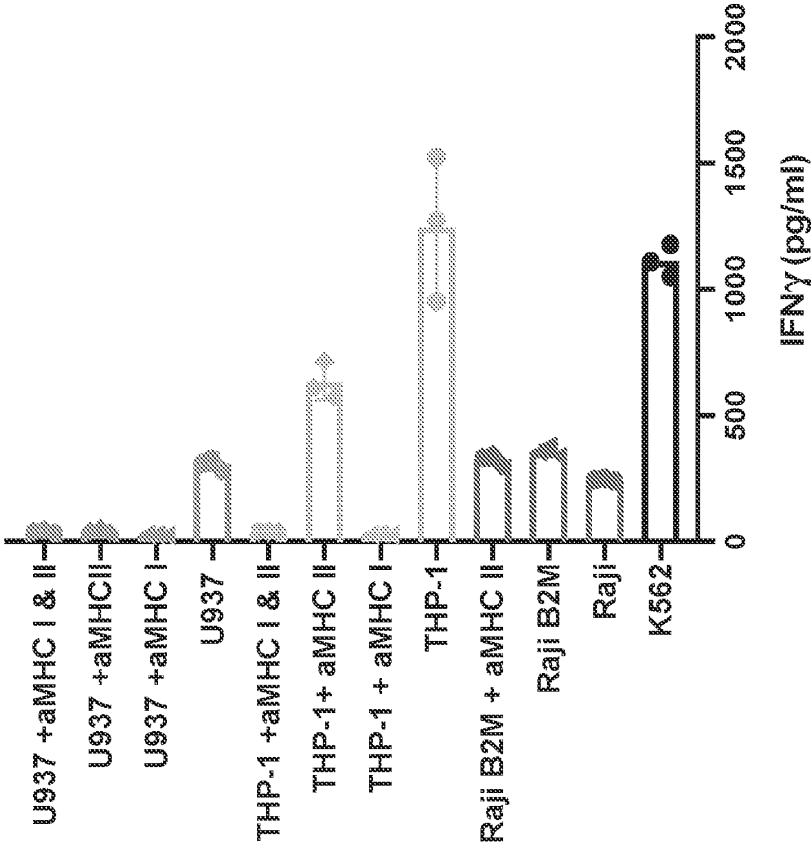


Figure 178

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M1152

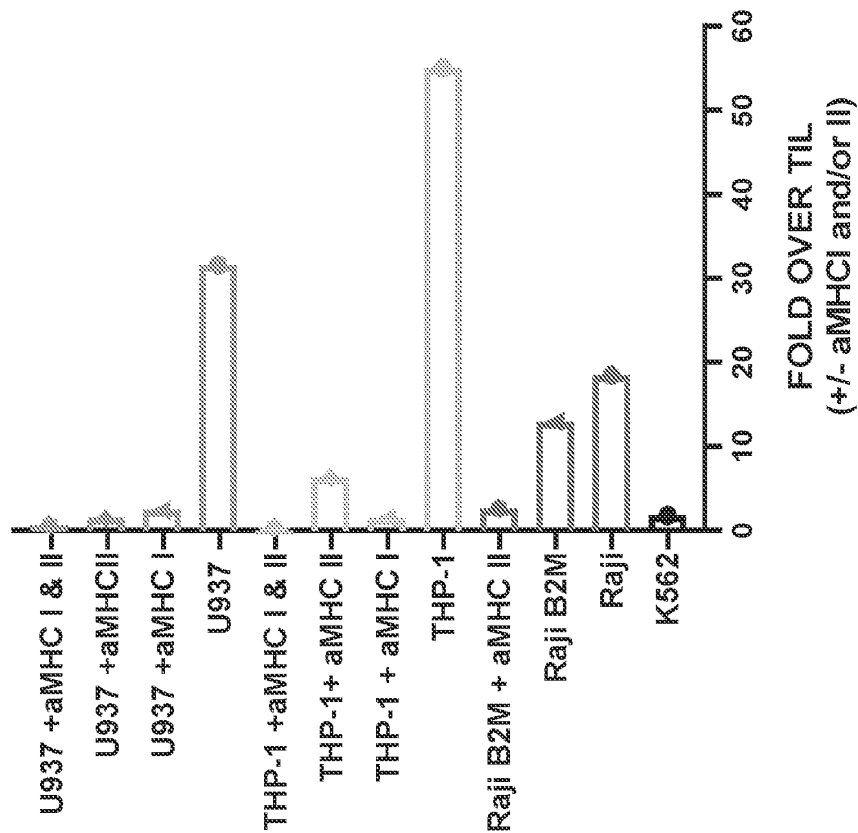


Figure 179

M1187

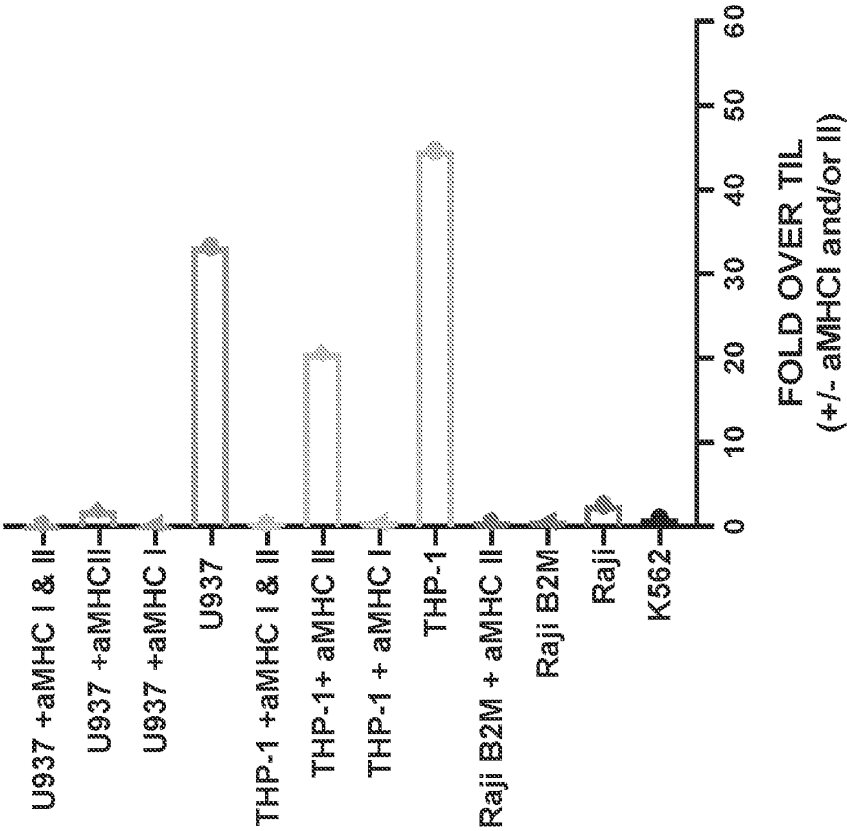


Figure 180

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M1164

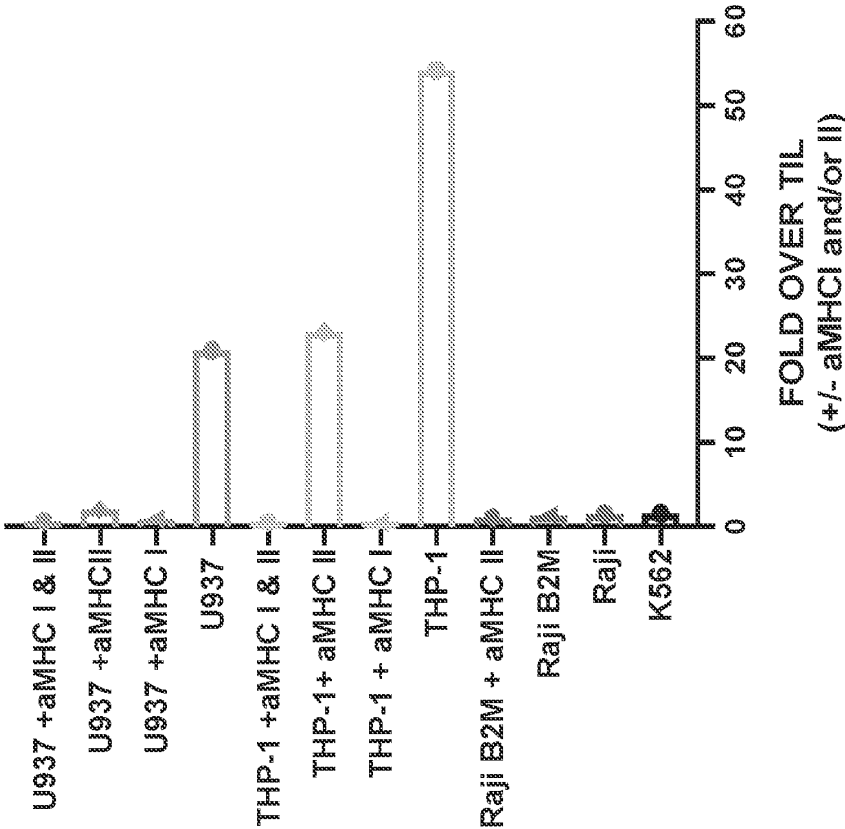


Figure 181

M1213

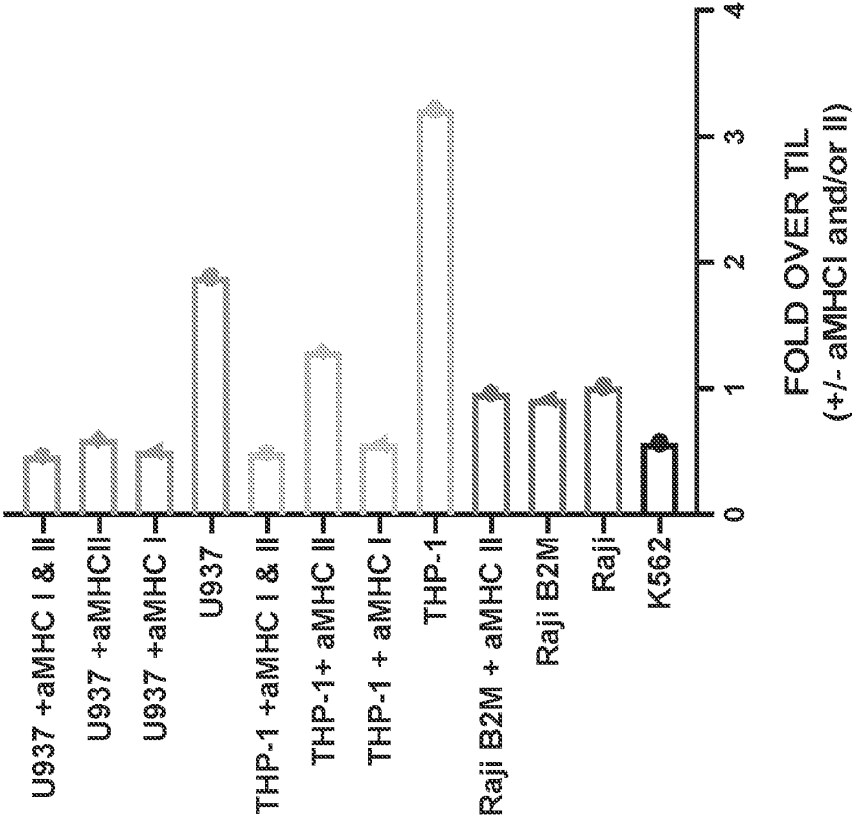


Figure 182

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M1214

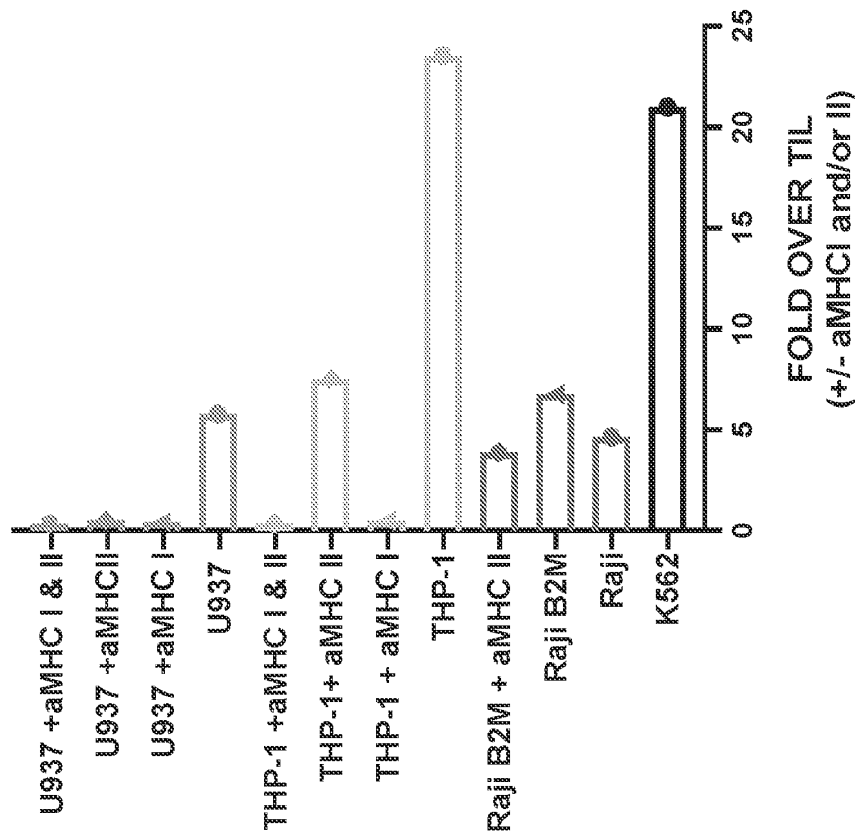


Figure 183

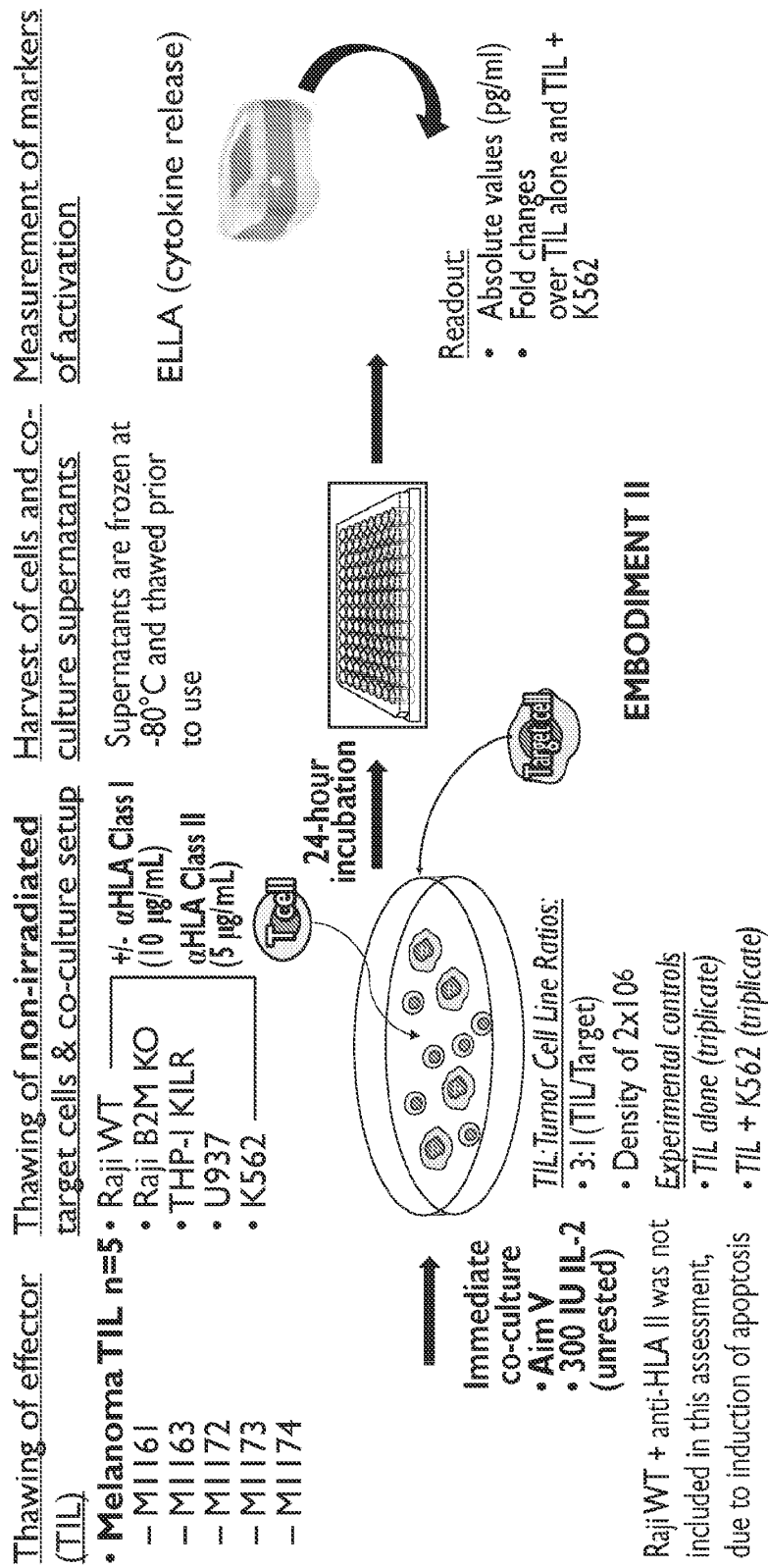


Figure 184

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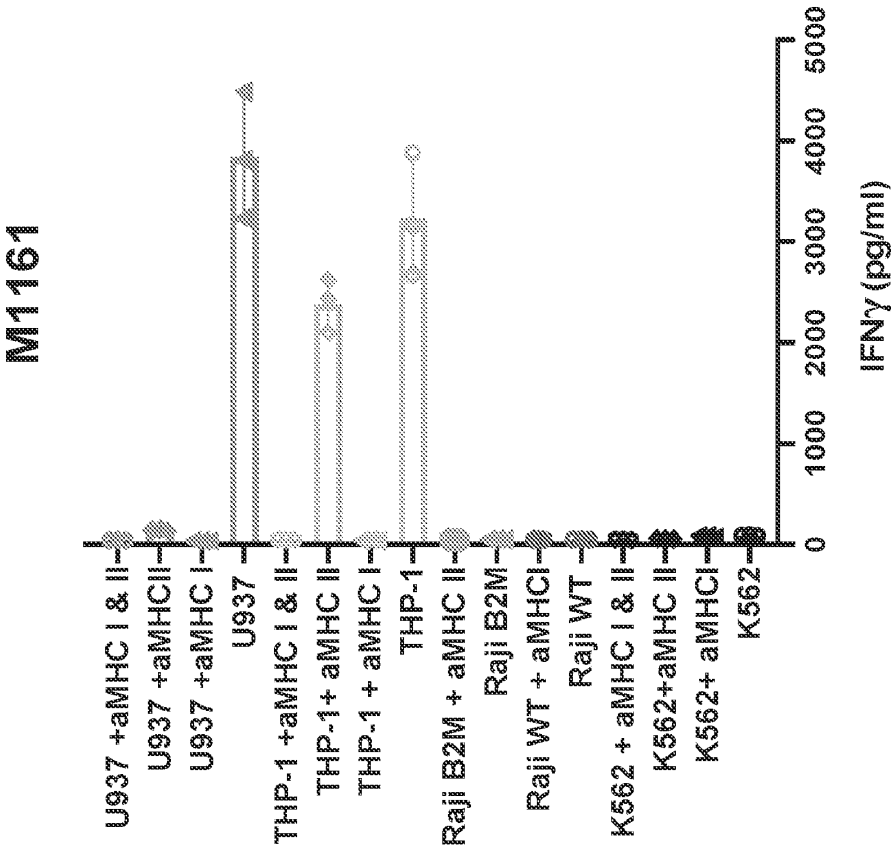


Figure 185

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M1163

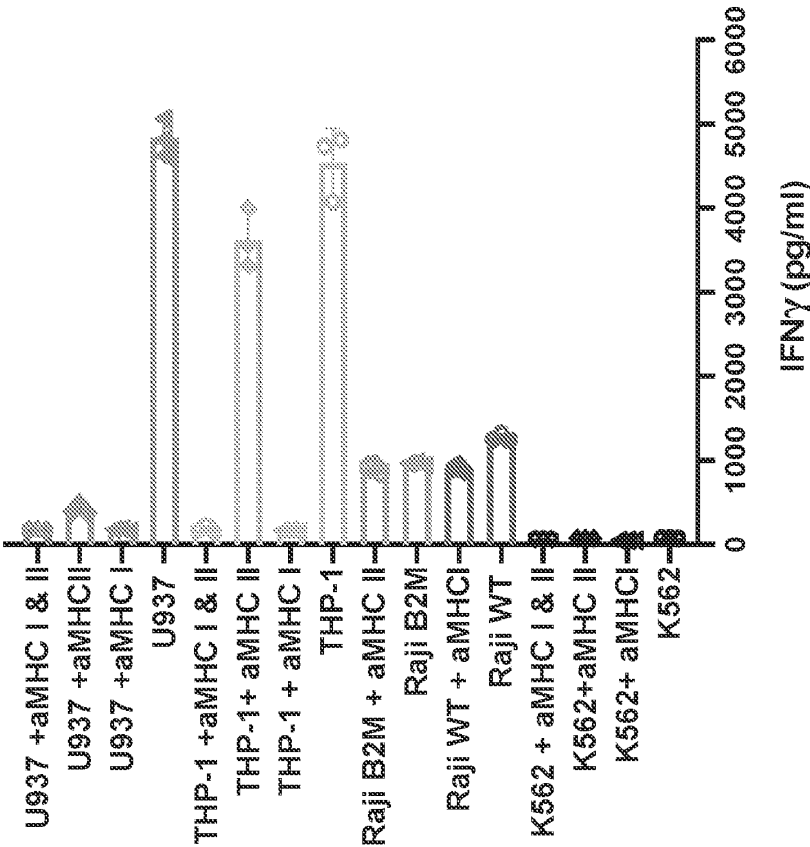


Figure 186

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M1172

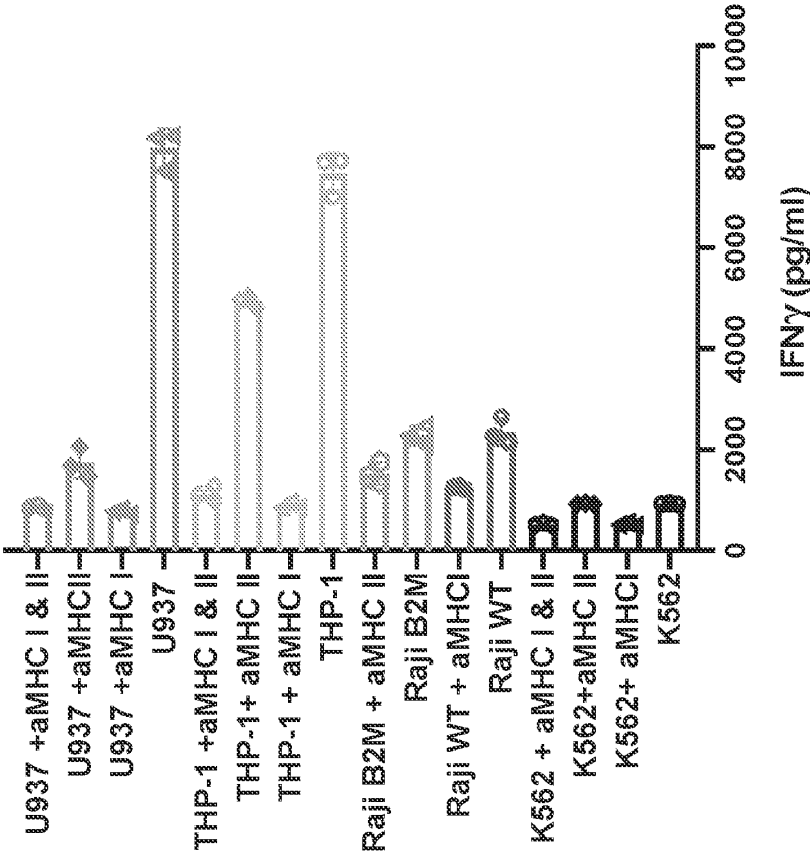


Figure 187

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M1173

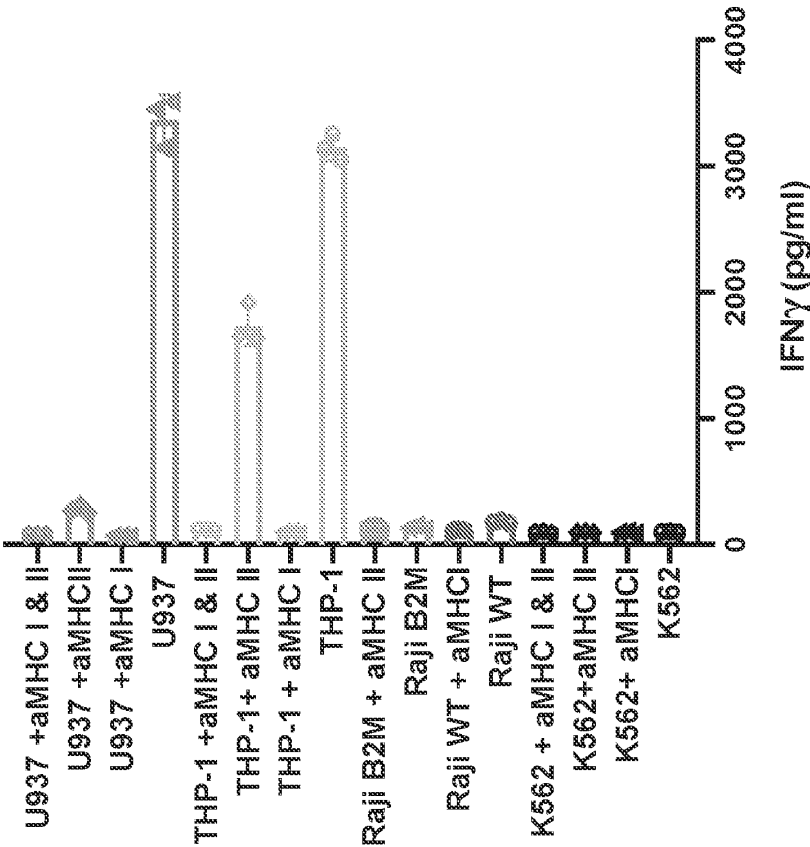


Figure 188

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M1174

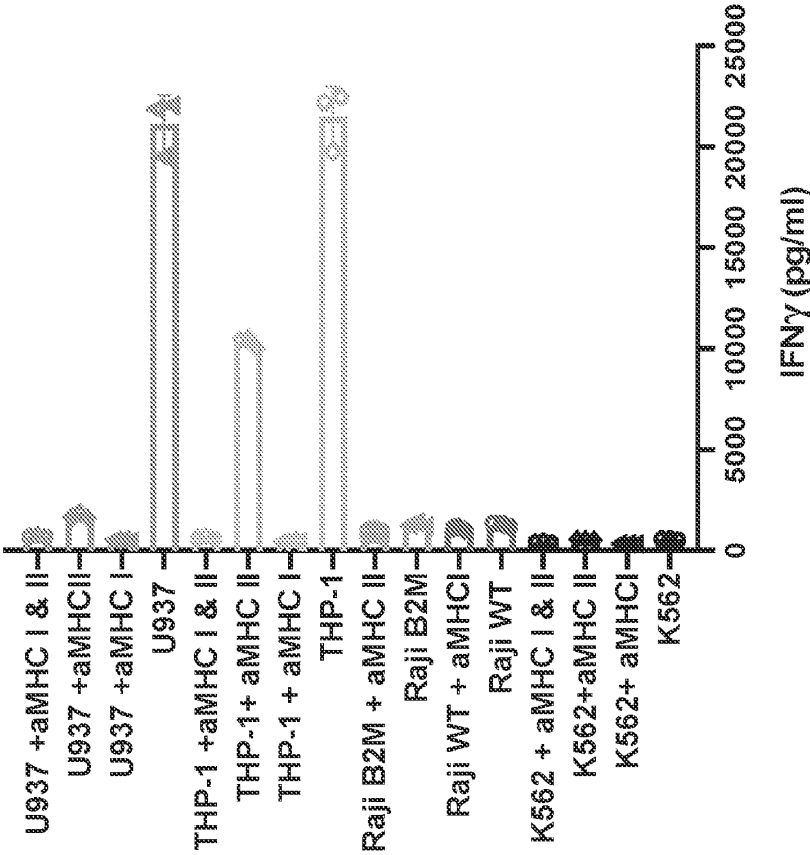


Figure 189

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M1161

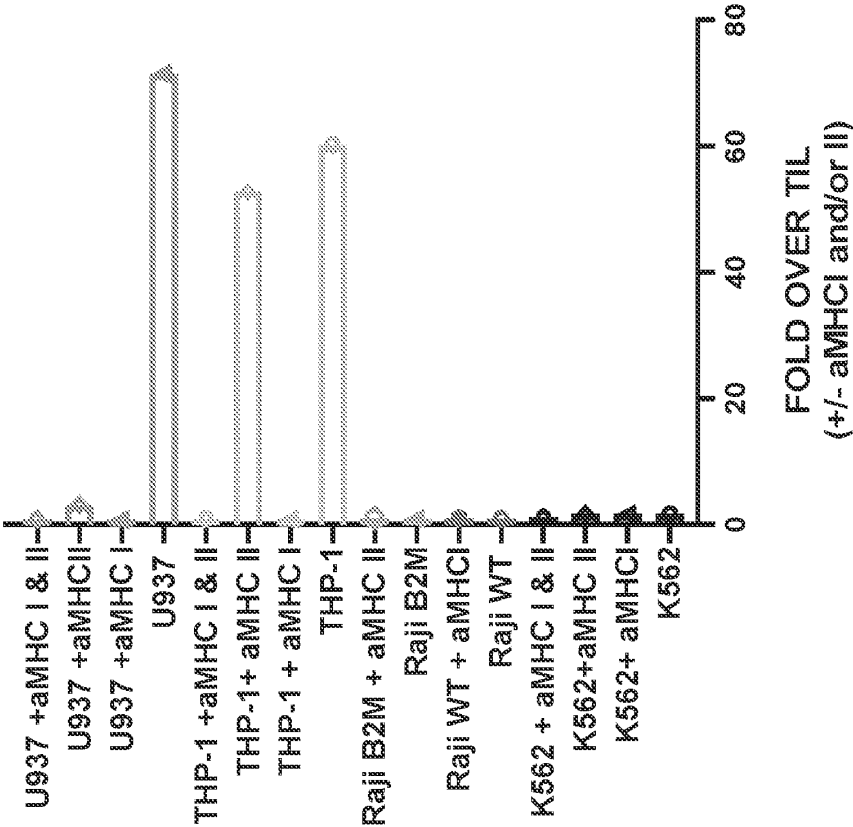


Figure 190

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M1163

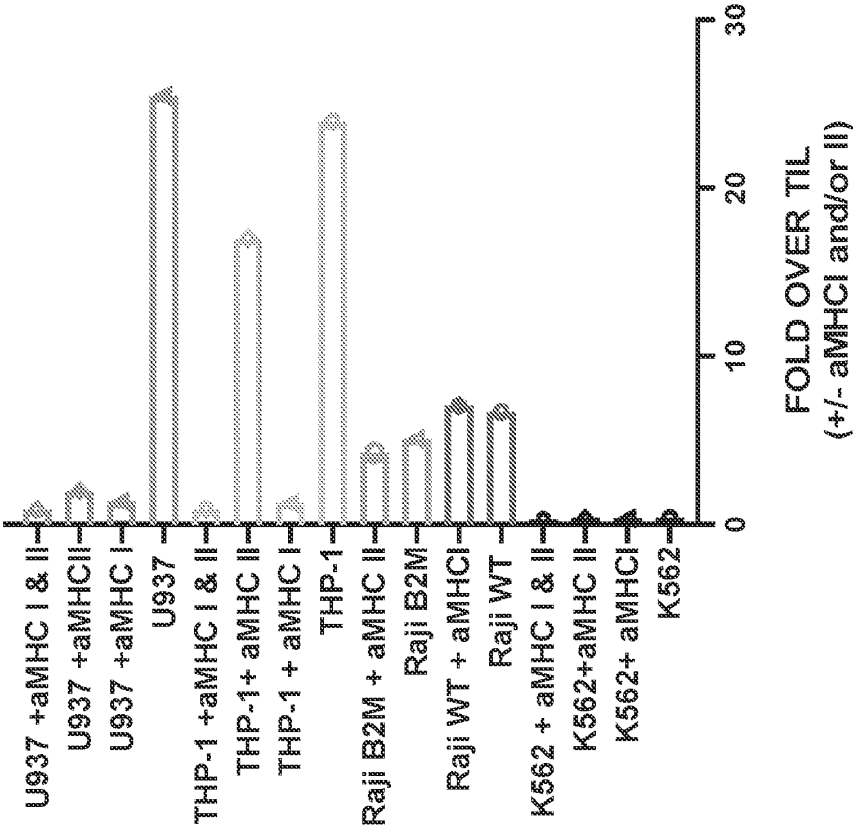


Figure 191

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M1172

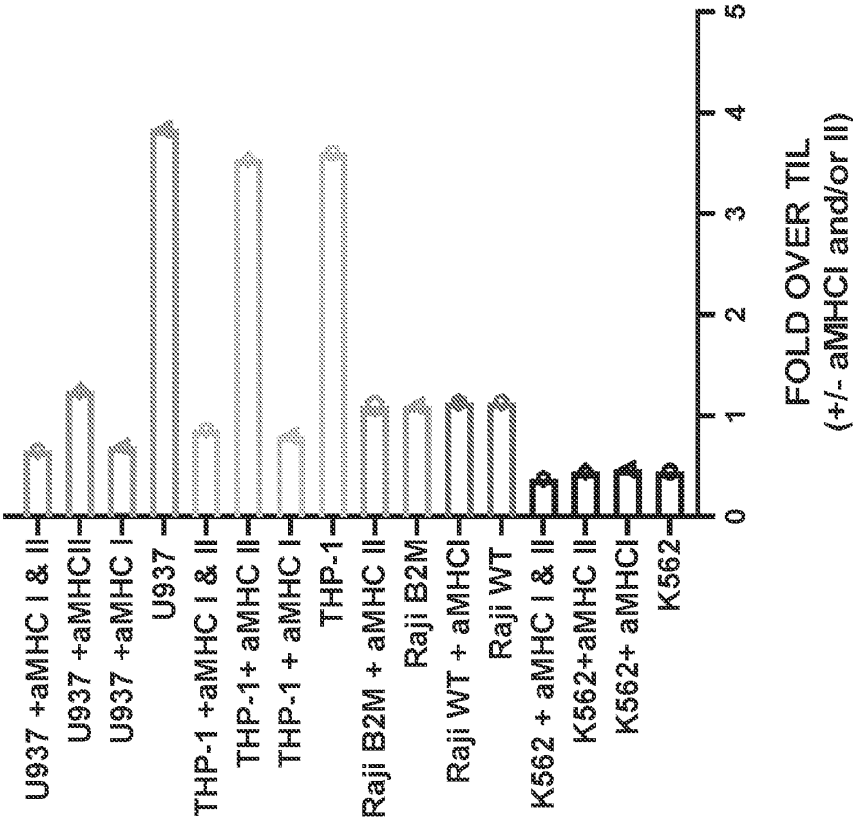


Figure 192

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M1173

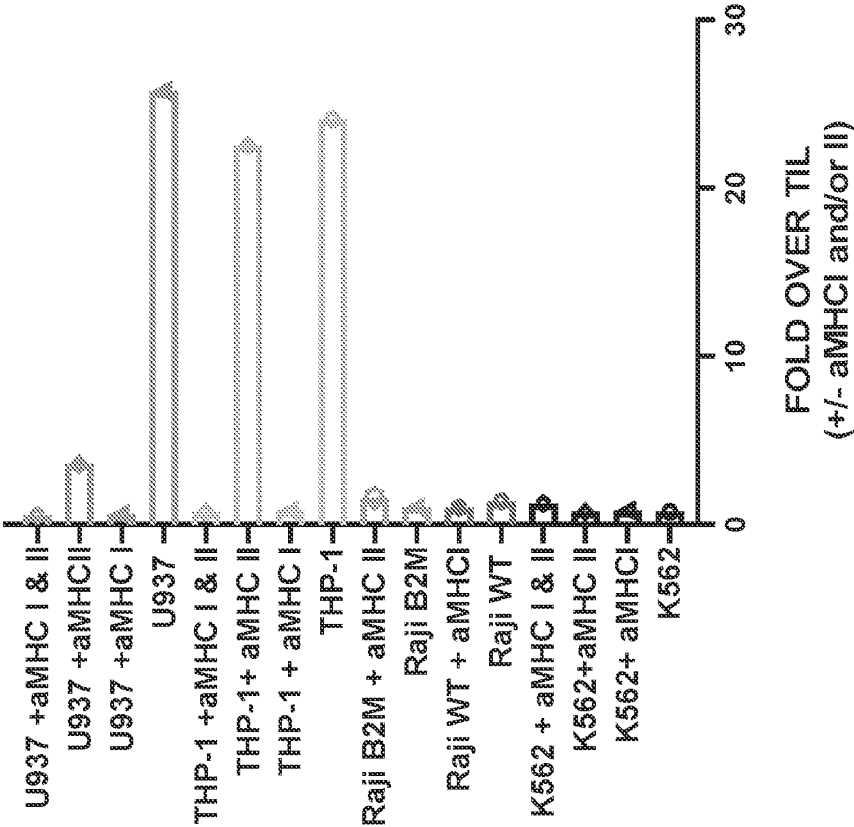


Figure 193

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M1174

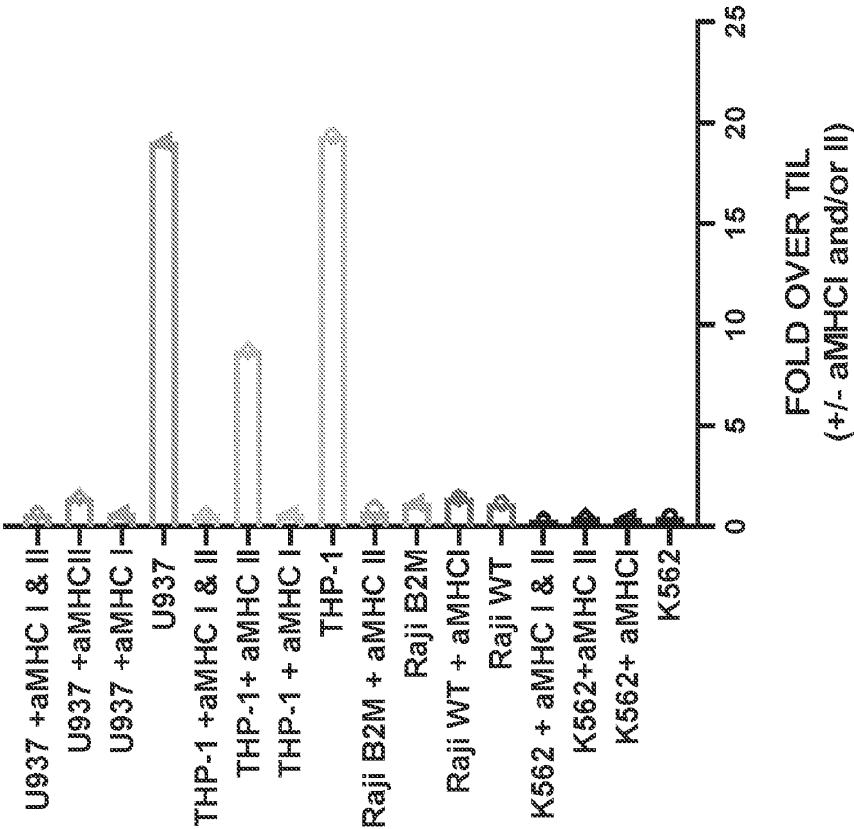


Figure 194

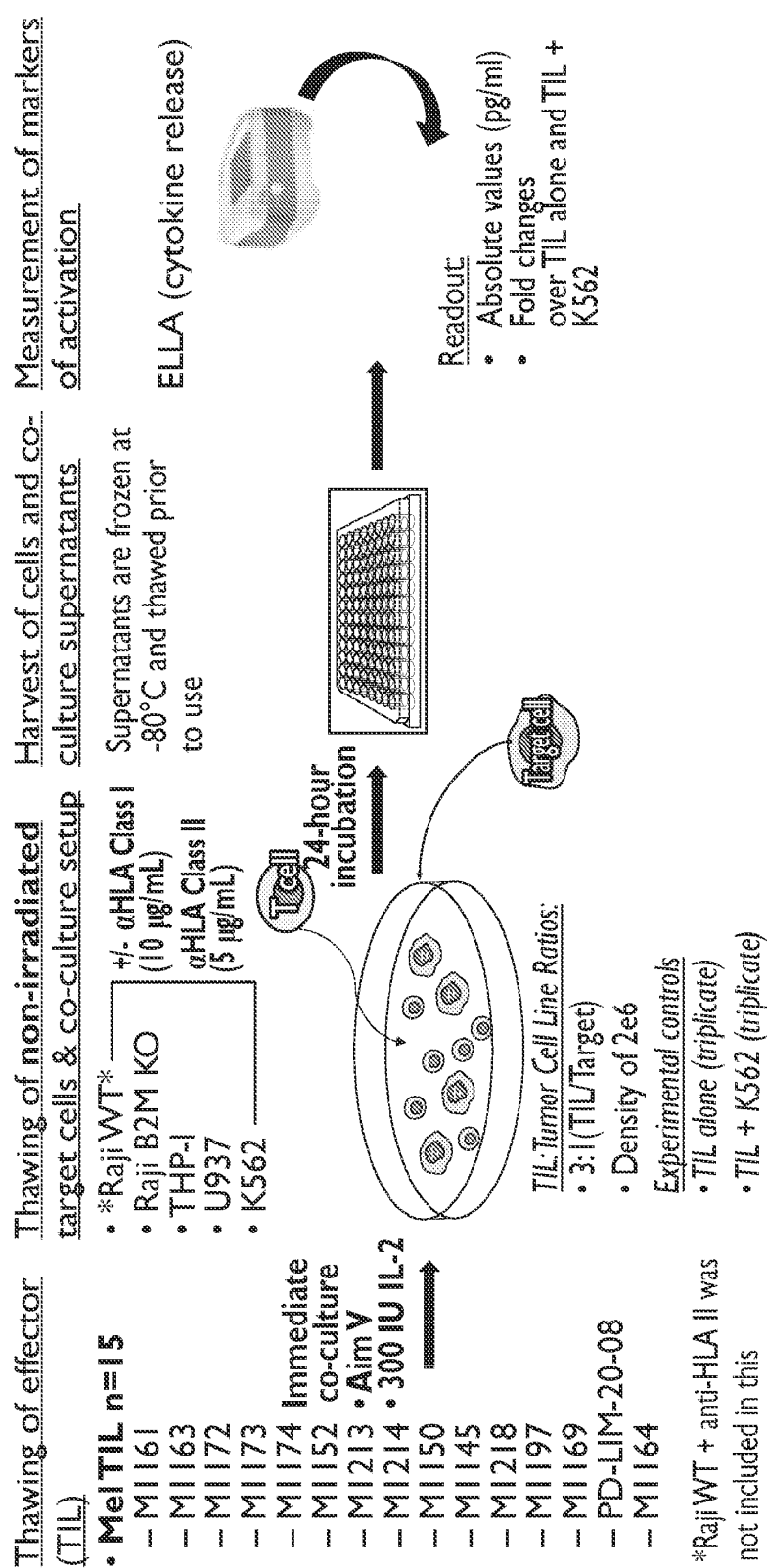


Figure 195

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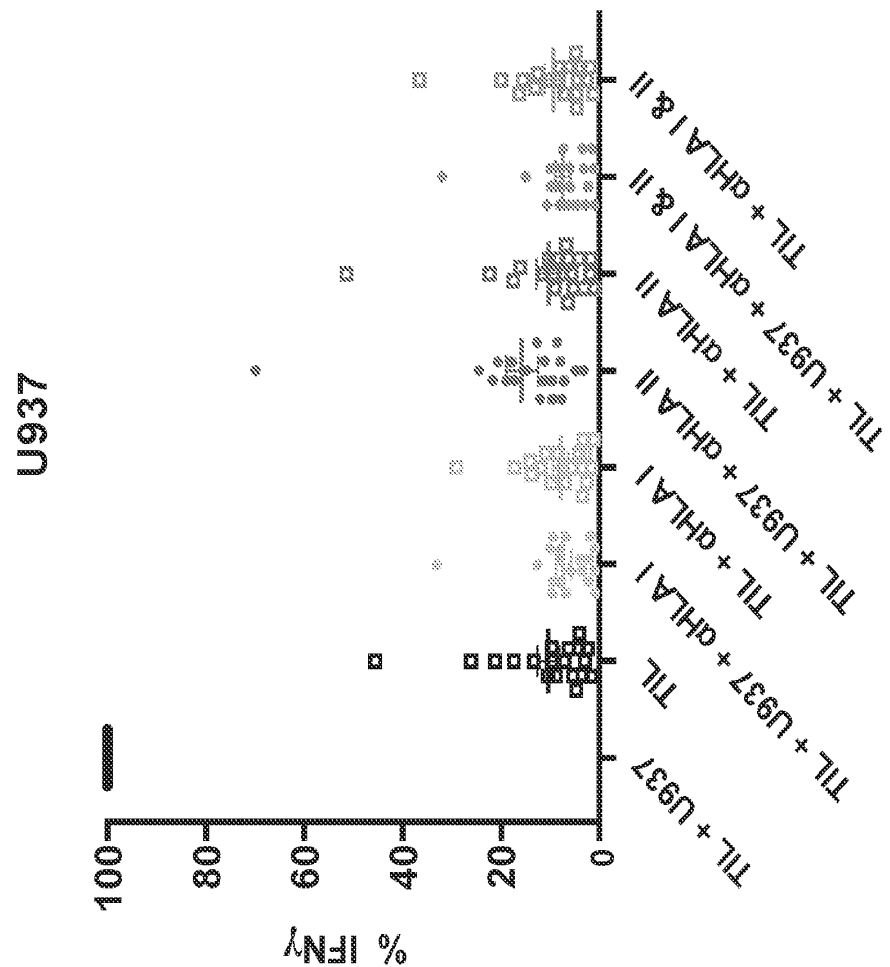


Figure 196

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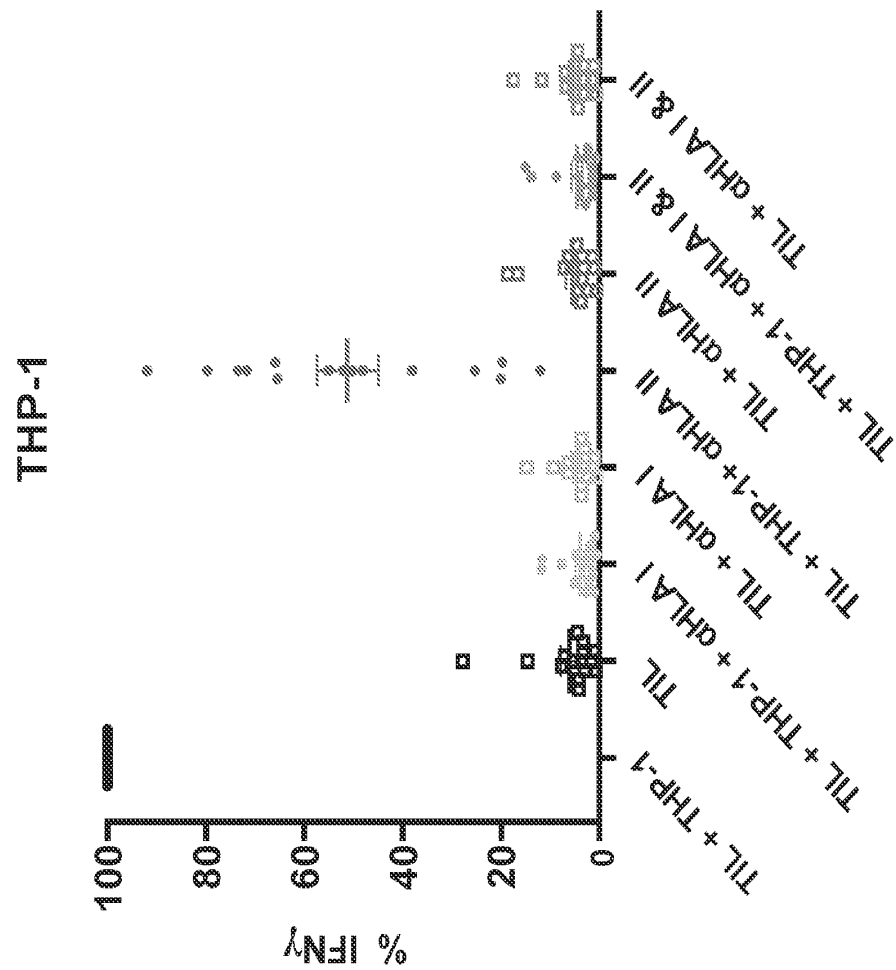


Figure 197

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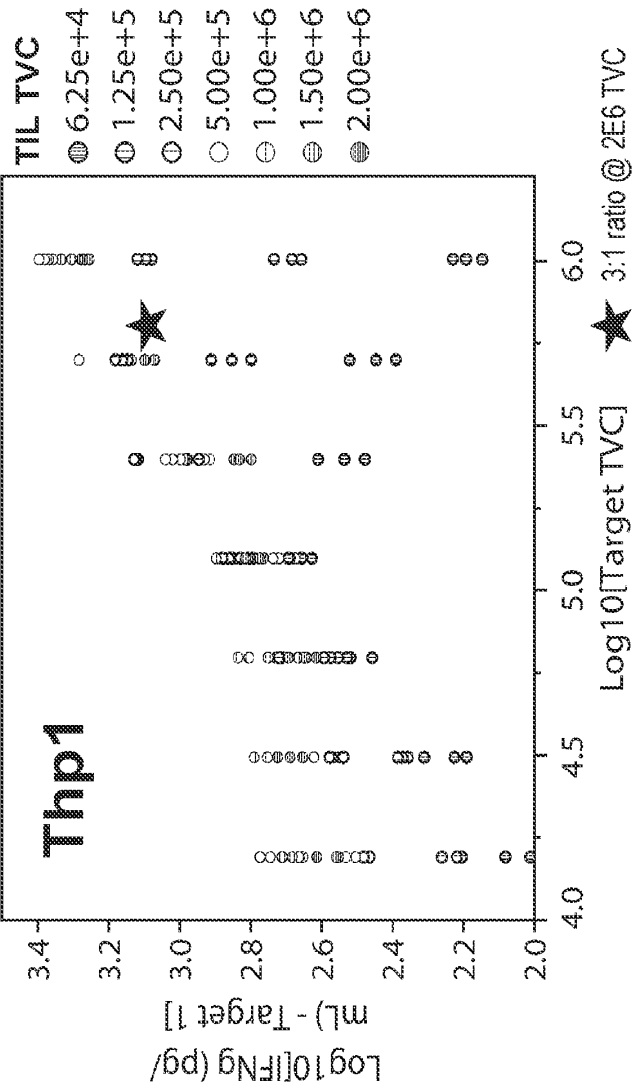


Figure 198

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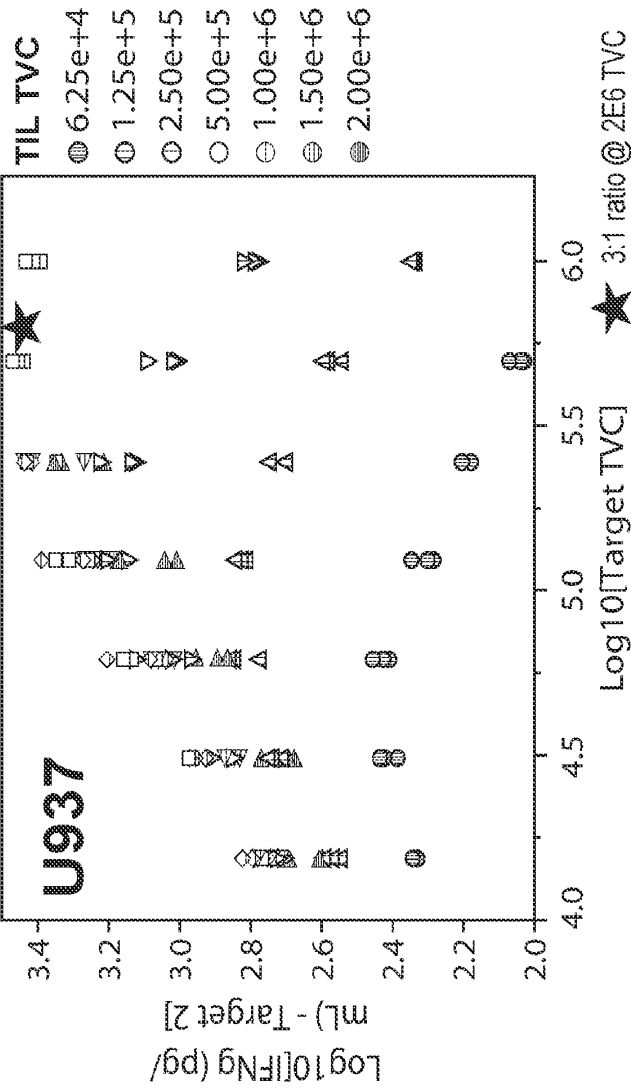


Figure 199

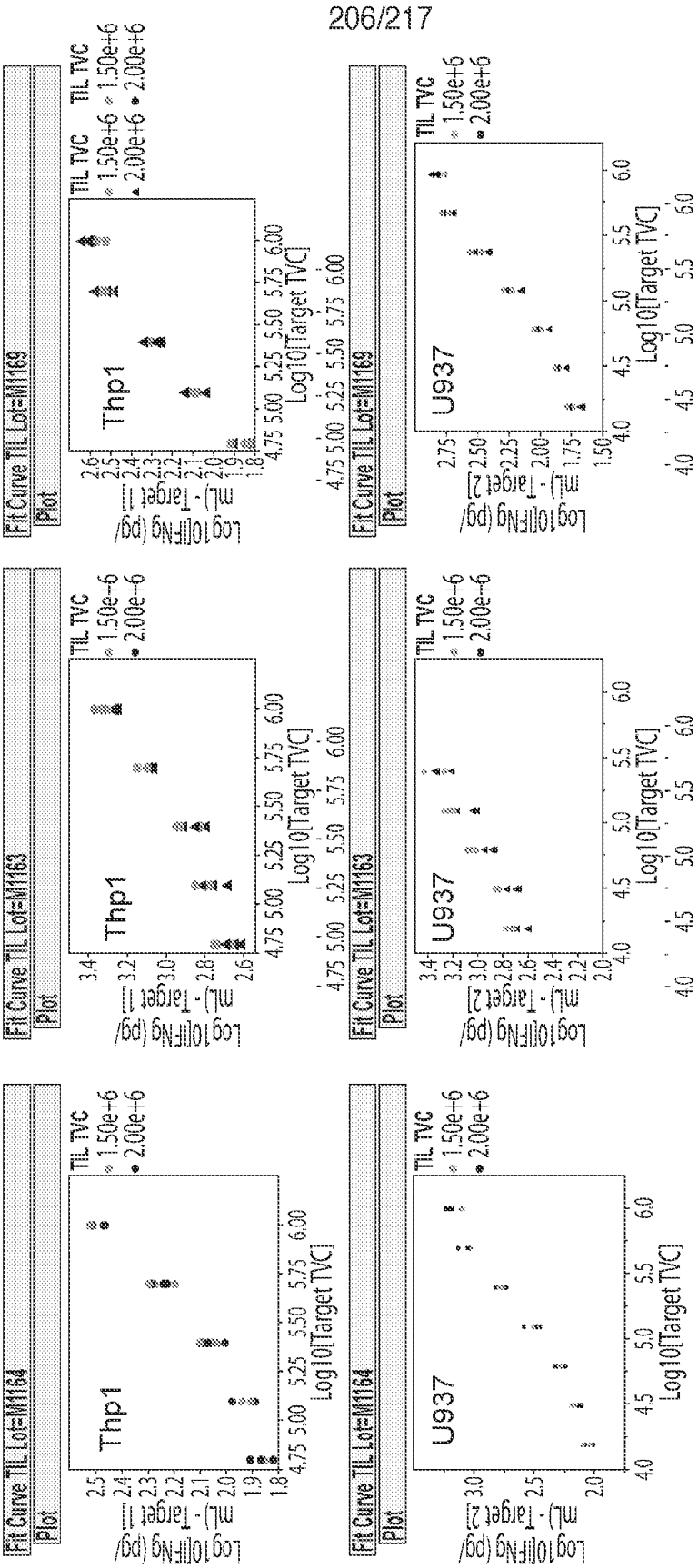


Figure 200

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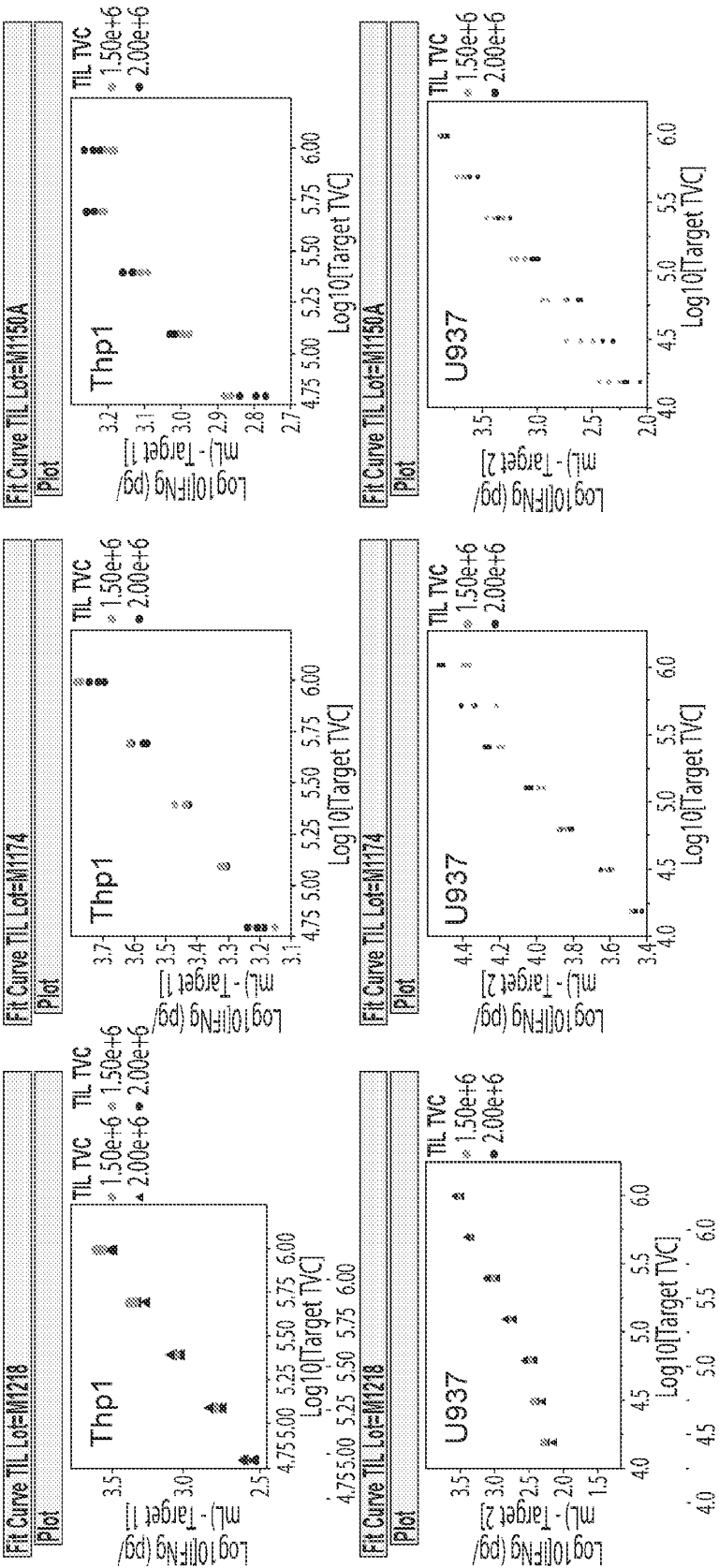


Figure 201

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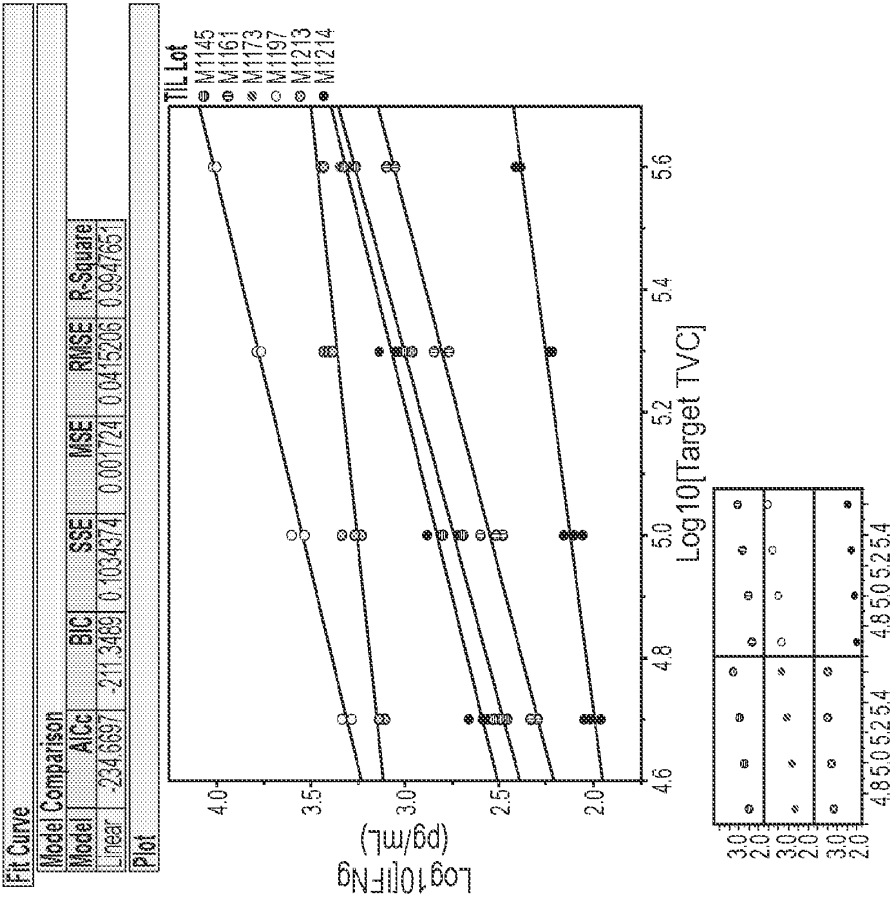


Figure 202

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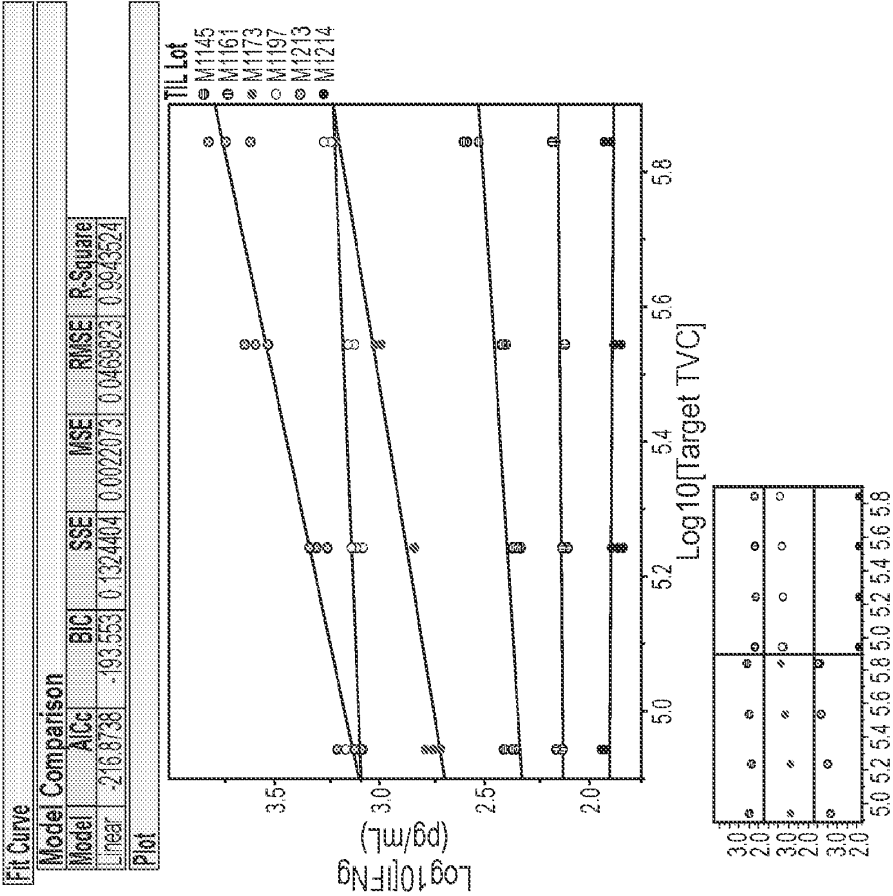
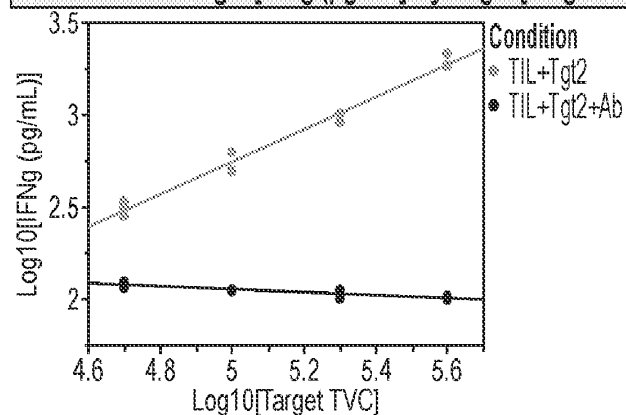


Figure 203

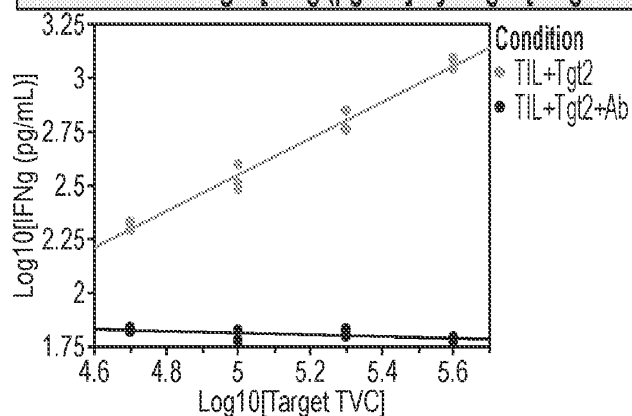
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Bivariate Fit of Log10[IFNg (pg/mL)] By Log10[Target TVC] TIL Lot=M1145



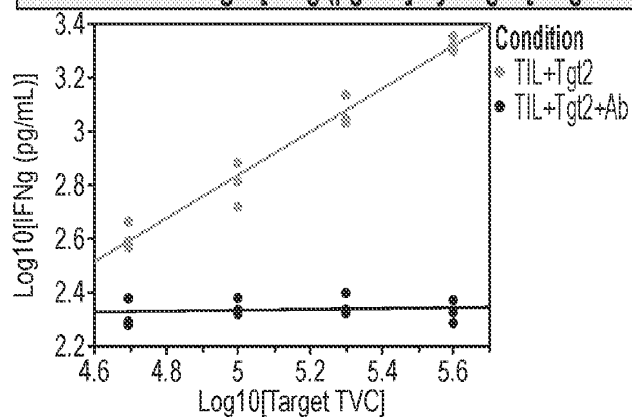
— Linear Fit Condition==TIL+Tgt2
— Linear Fit Condition==TIL+Tgt2+Ab

Bivariate Fit of Log10[IFNg (pg/mL)] By Log10[Target TVC] TIL Lot=M1161



— Linear Fit Condition==TIL+Tgt2
— Linear Fit Condition==TIL+Tgt2+Ab

Bivariate Fit of Log10[IFNg (pg/mL)] By Log10[Target TVC] TIL Lot=M1173

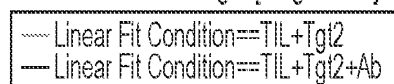
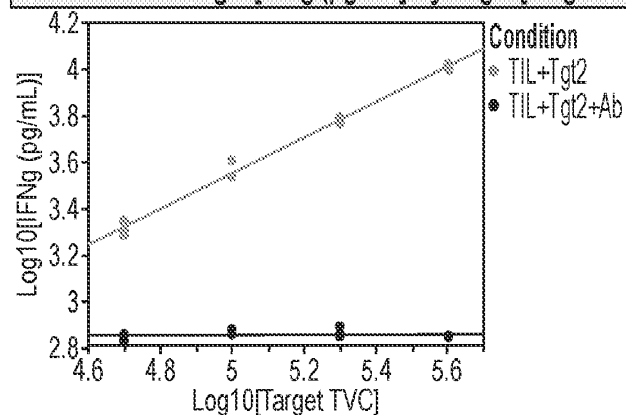


— Linear Fit Condition==TIL+Tgt2
— Linear Fit Condition==TIL+Tgt2+Ab

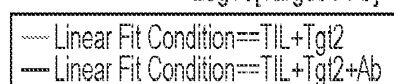
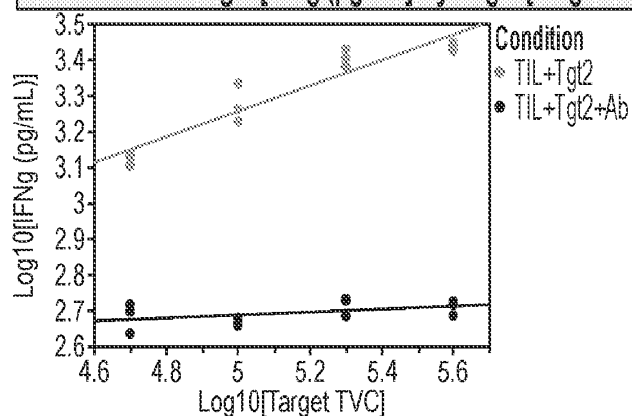
Figure 204

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Bivariate Fit of Log10[IFNg (pg/mL)] By Log10[Target TVC] TIL Lot=M1197



Bivariate Fit of Log10[IFNg (pg/mL)] By Log10[Target TVC] TIL Lot=M1213



Bivariate Fit of Log10[IFNg (pg/mL)] By Log10[Target TVC] TIL Lot=M1214

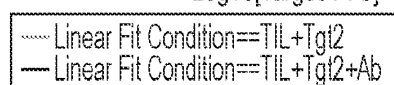
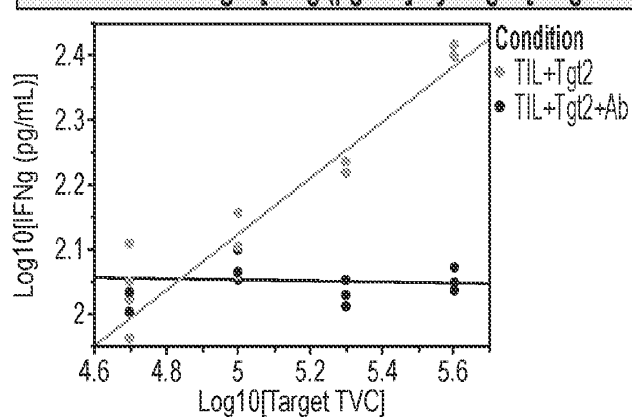


Figure 205

SUBSTITUTE SHEET (RULE 26)

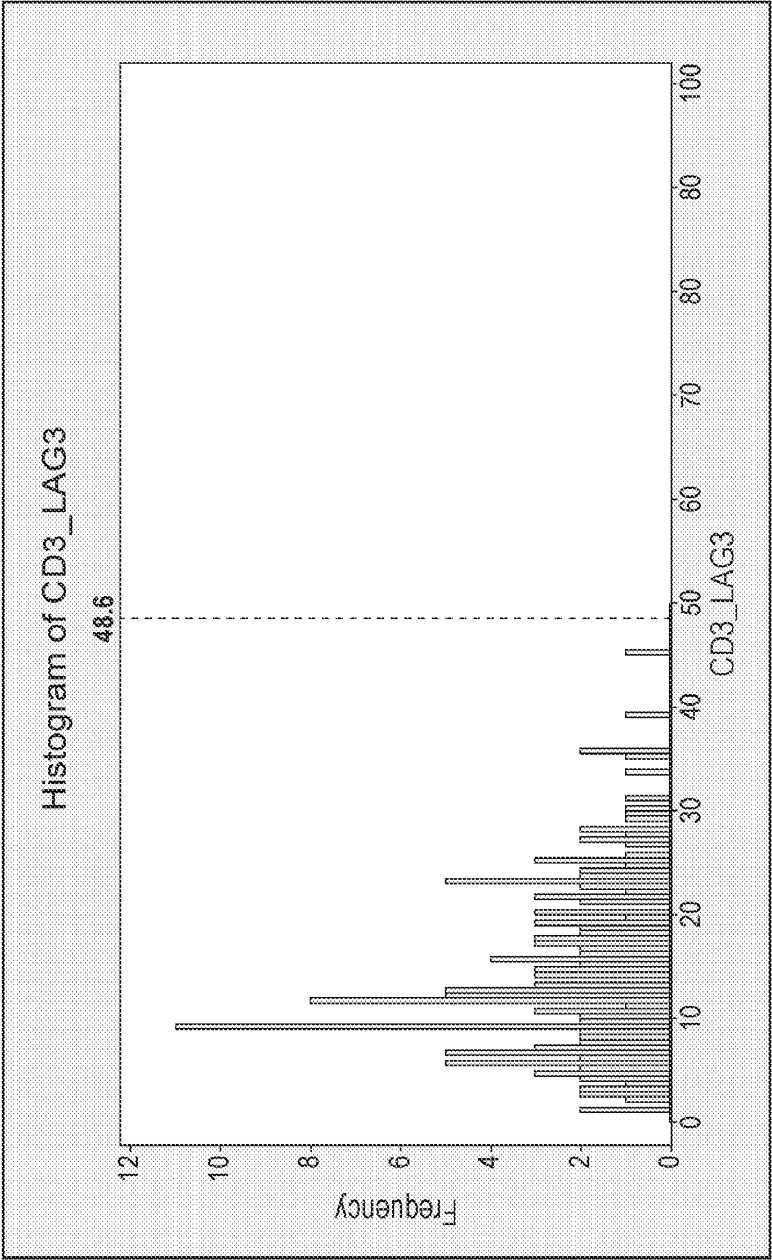


Figure 206

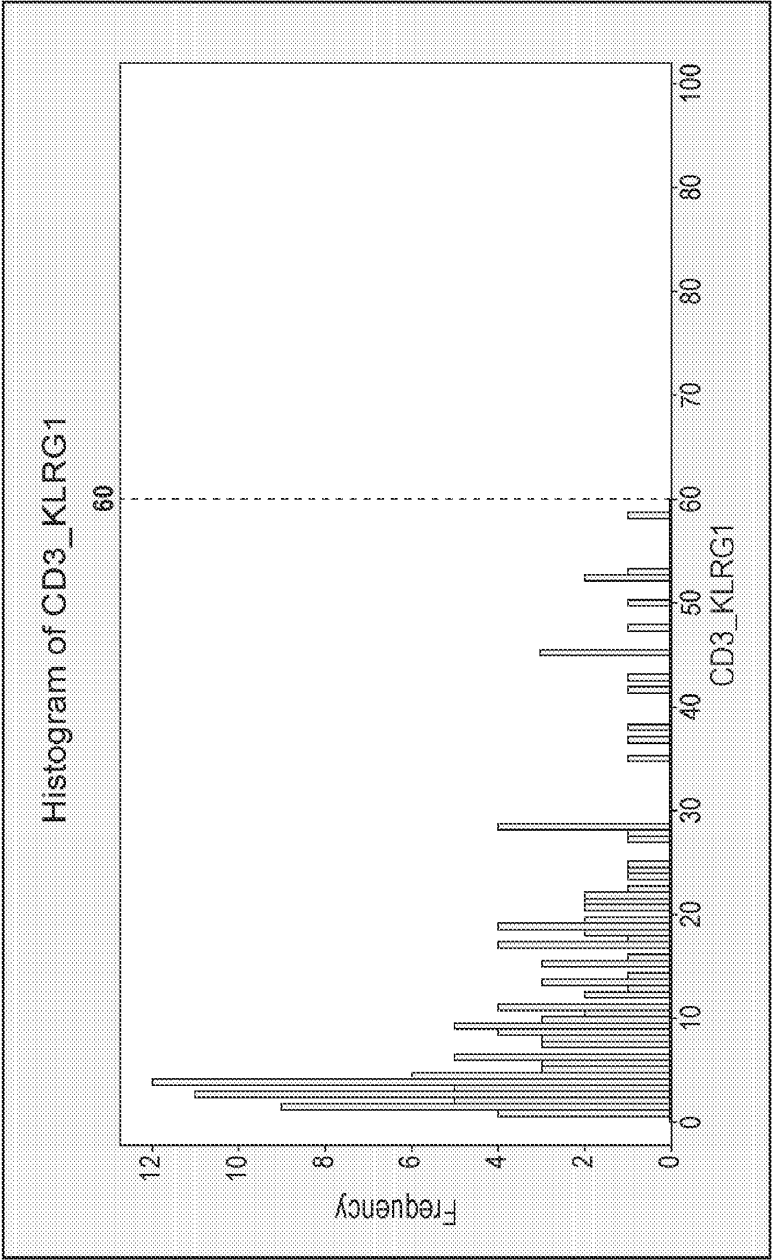


Figure 207

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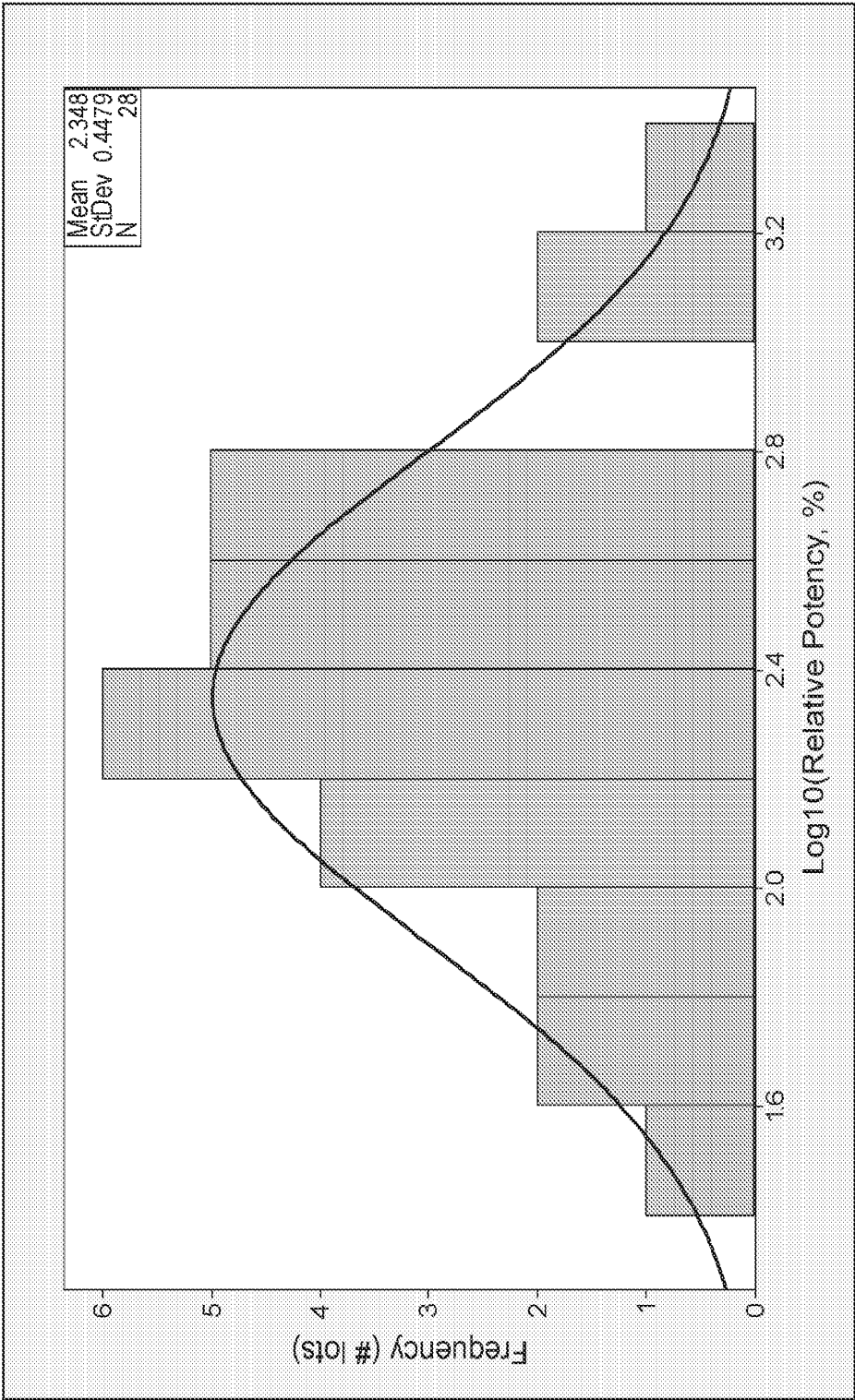


Figure 208

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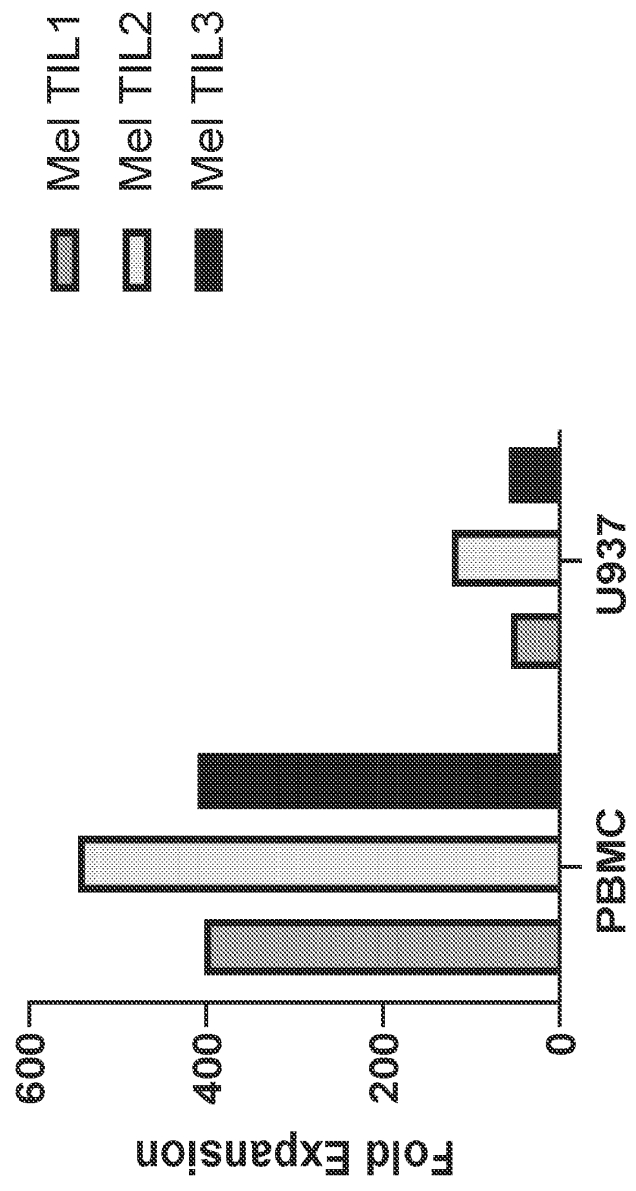


Figure 209

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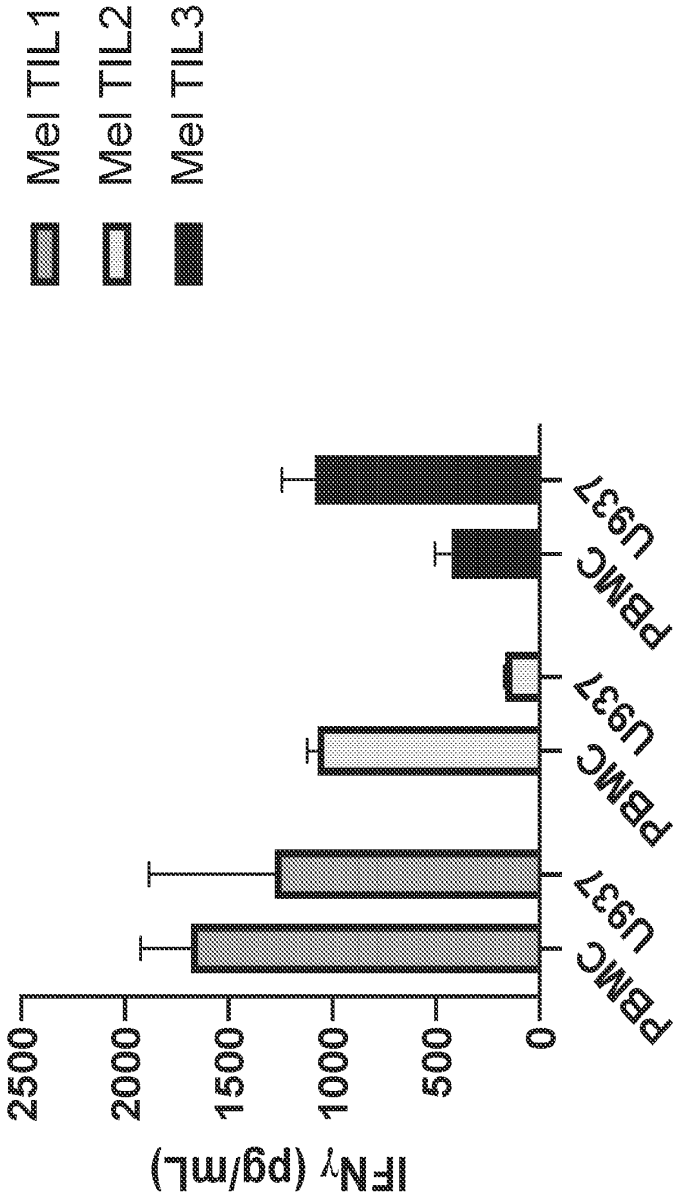


Figure 210

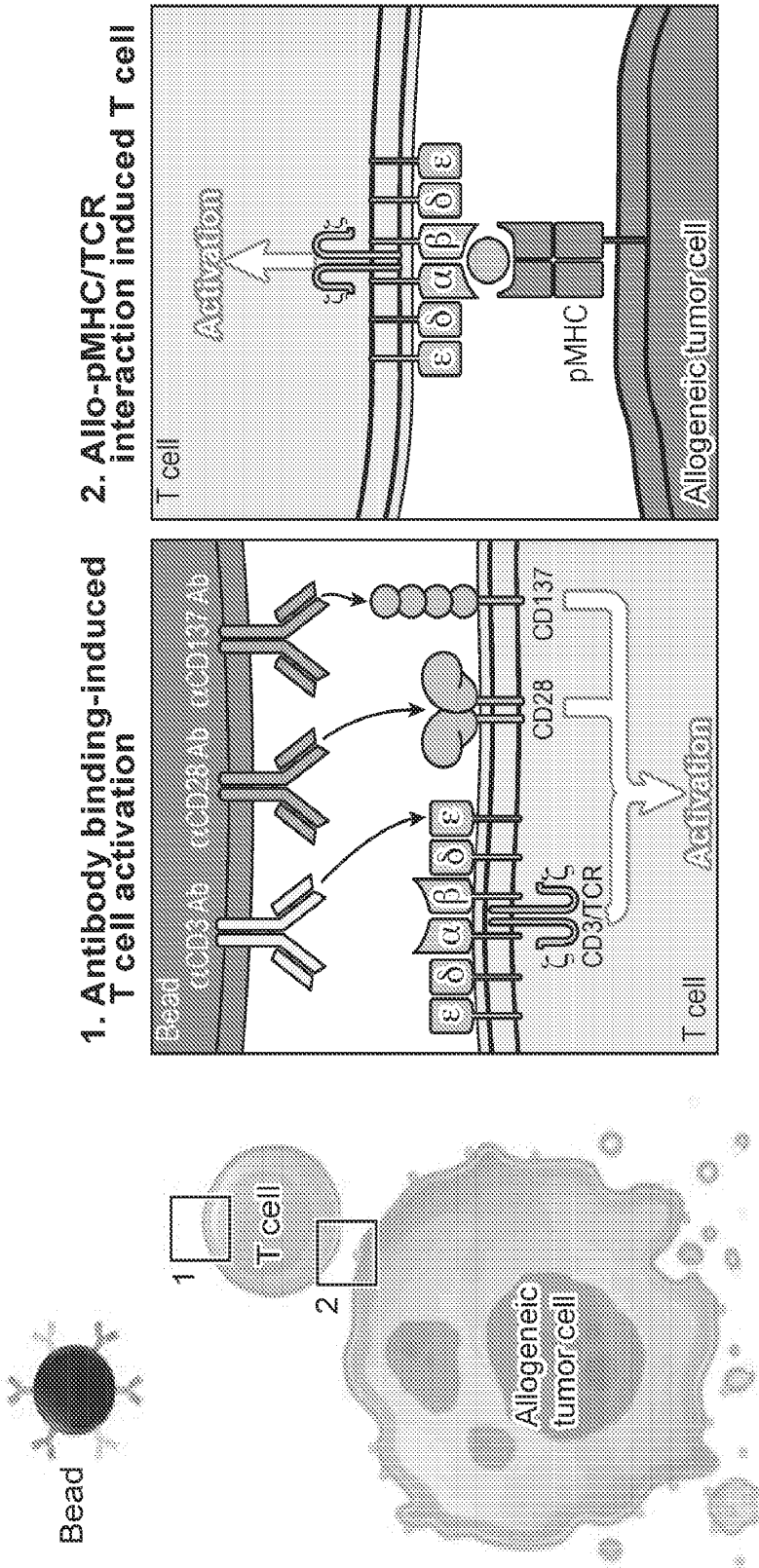


Figure 211