

Figure 1

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)

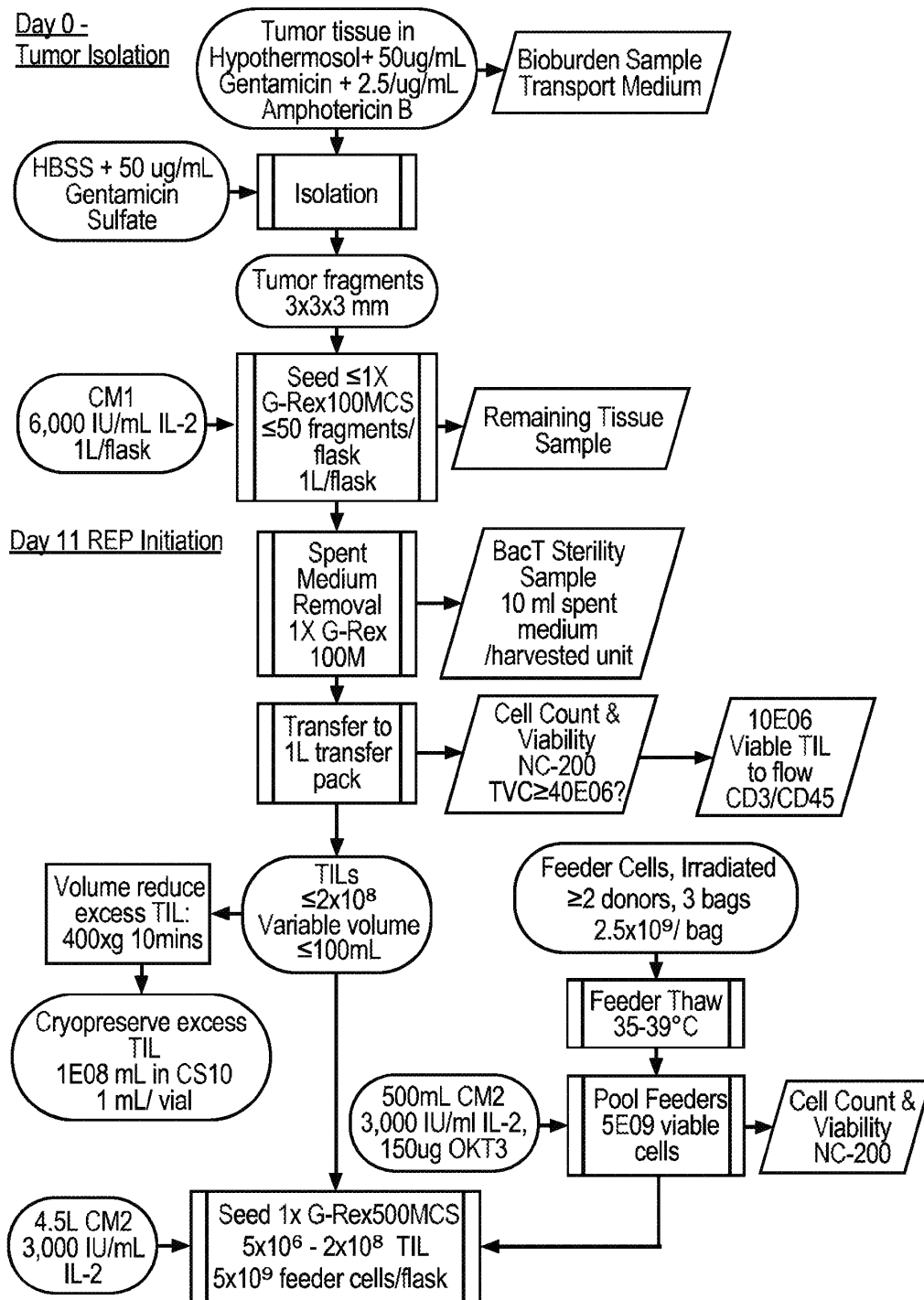


Figure 2B

Figure 2A

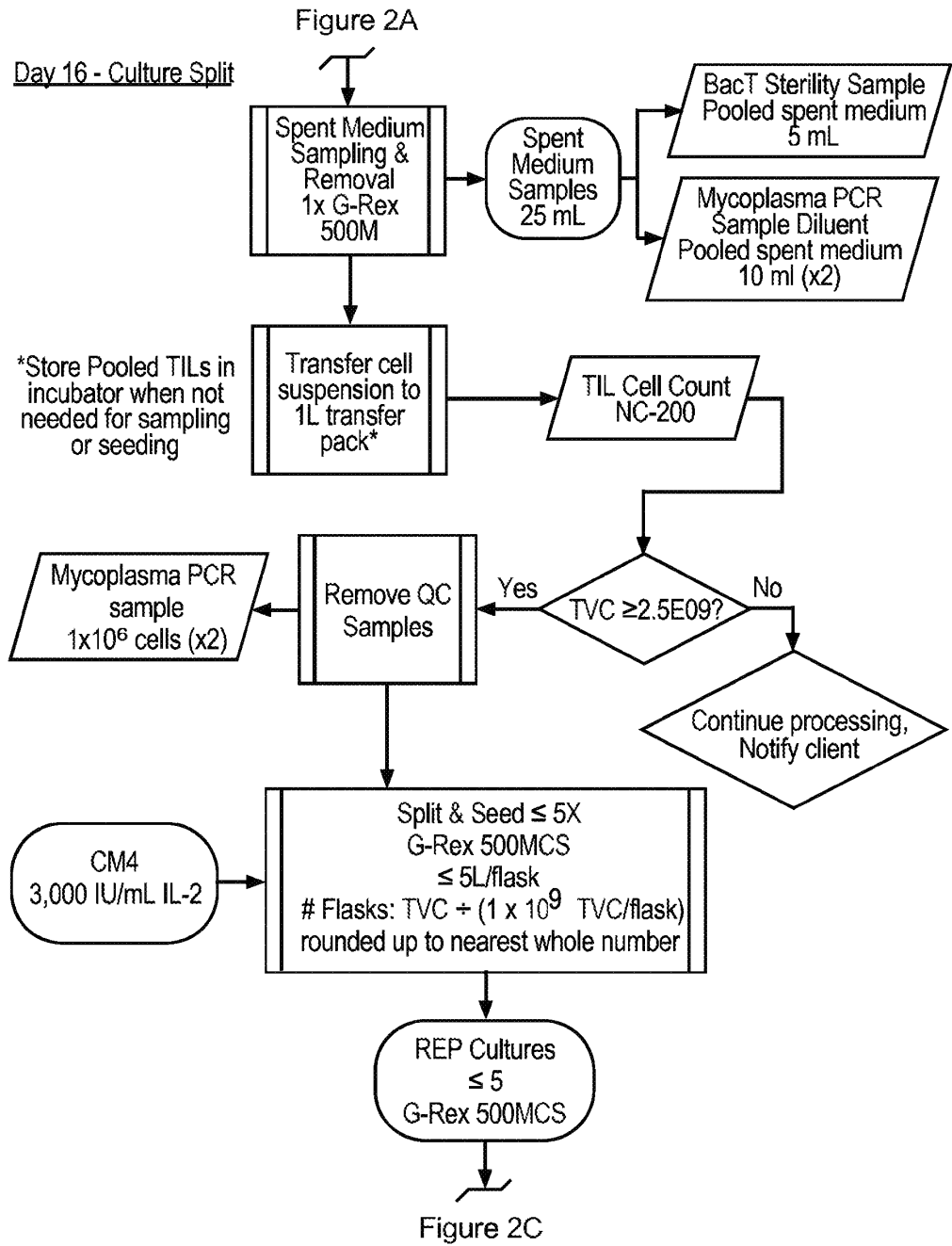


Figure 2B

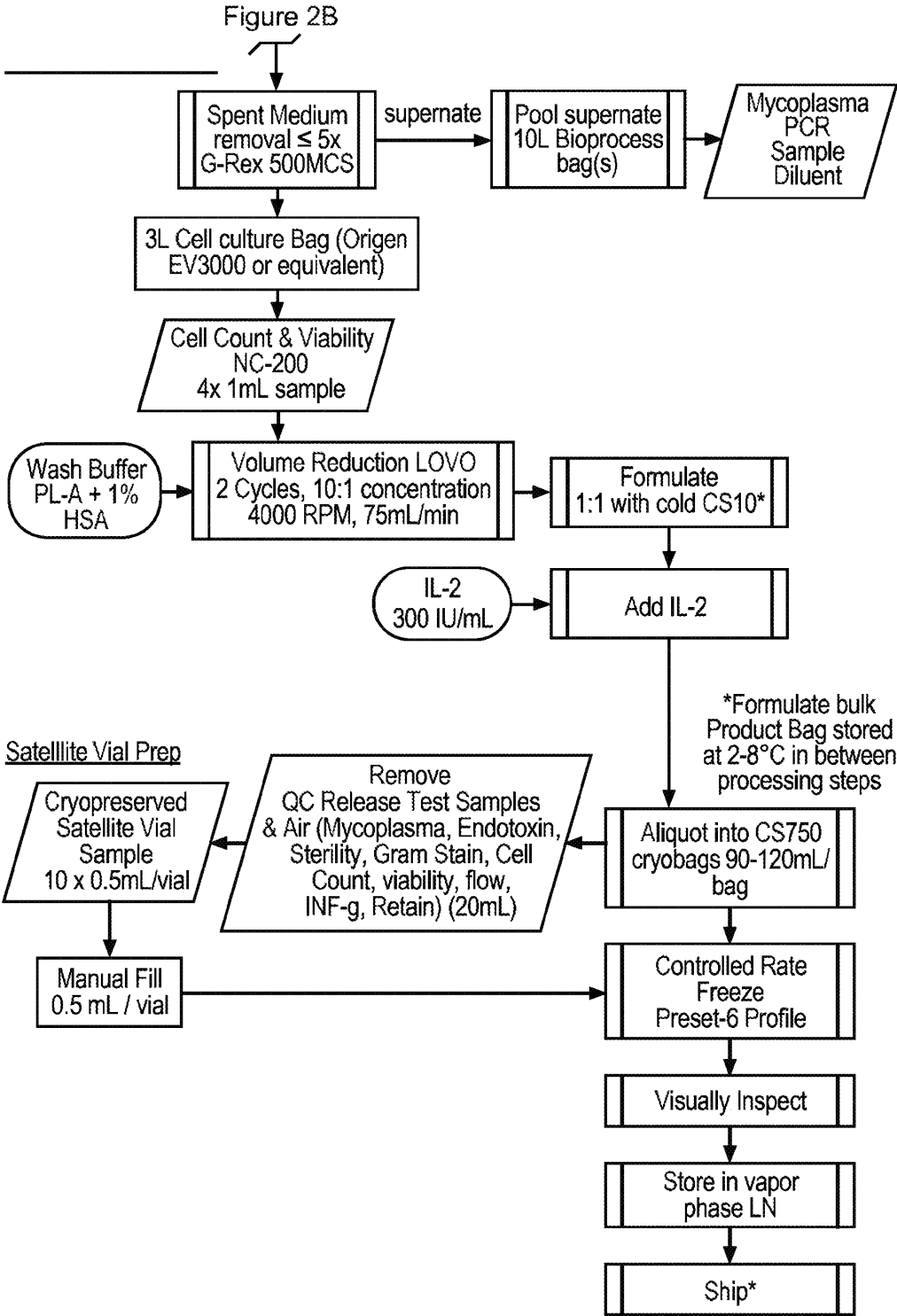


Figure 2C

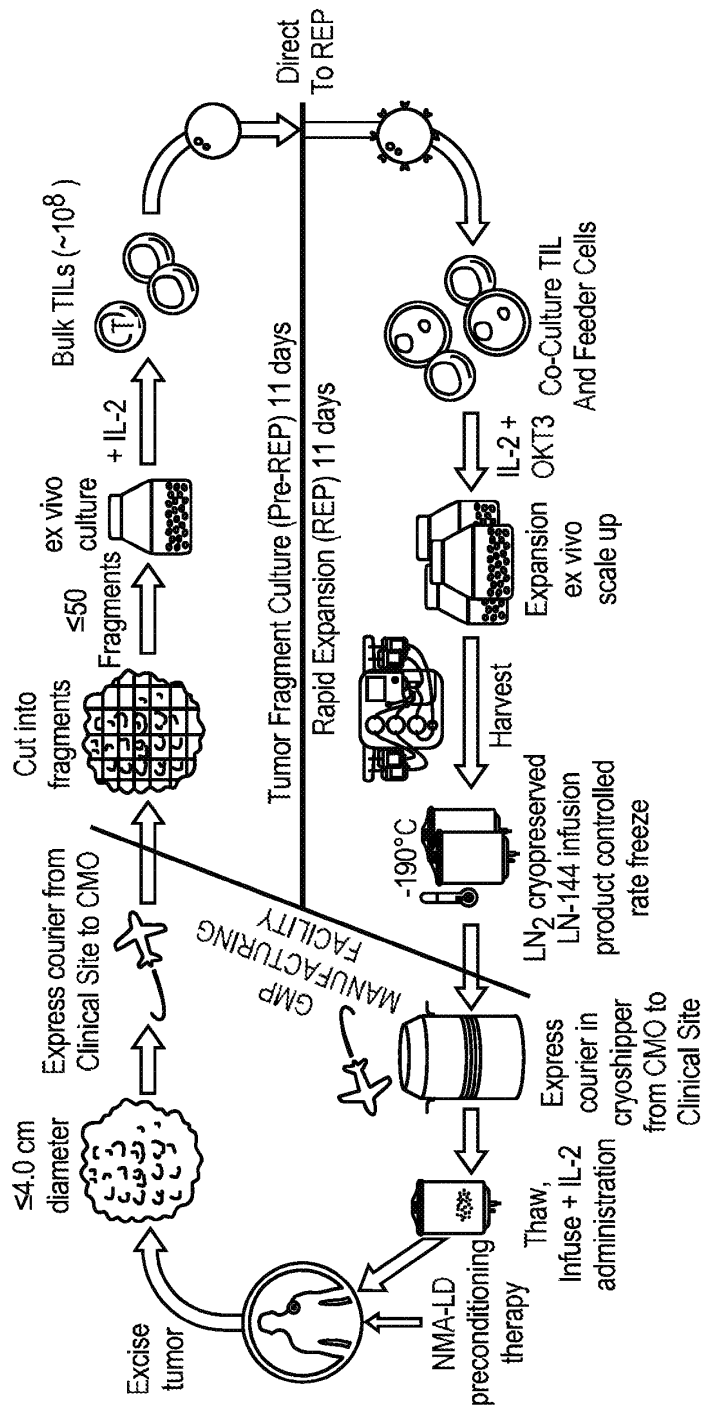


Figure 3

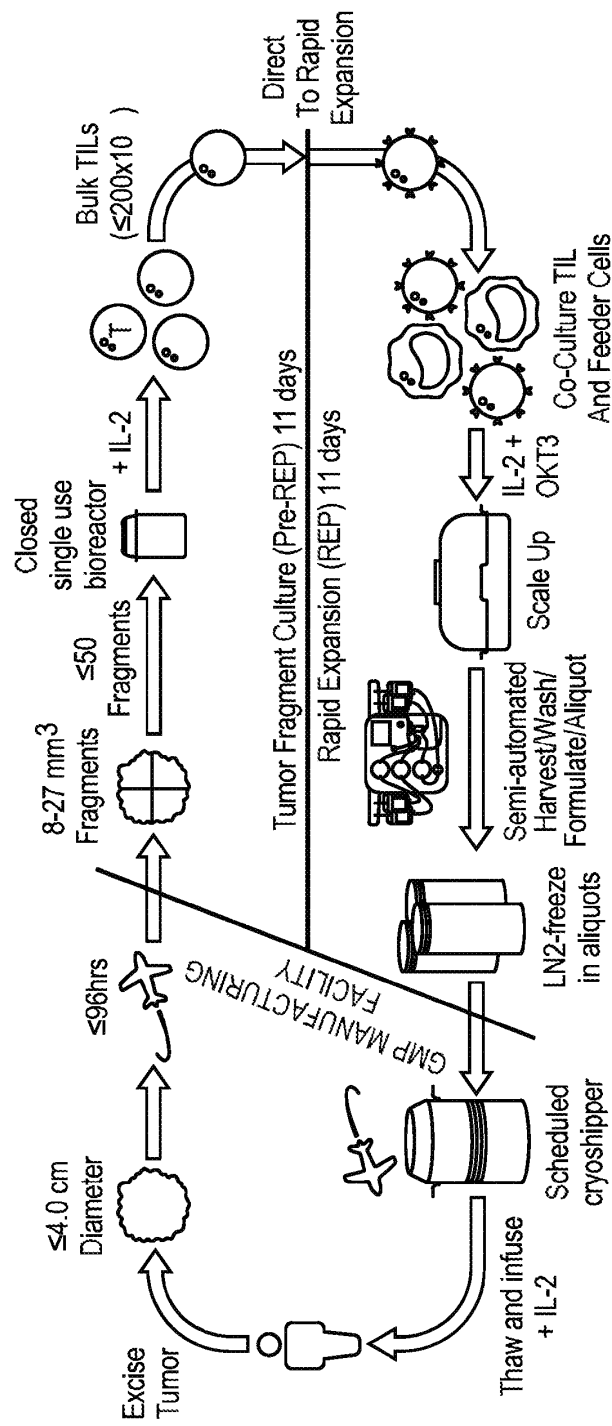


Figure 4

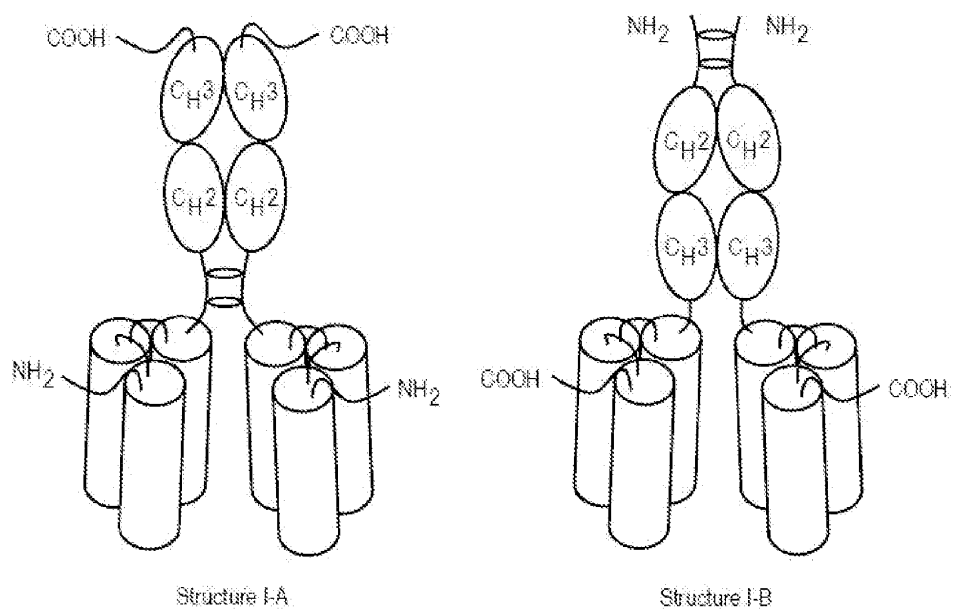
Figure 5

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, and 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 6

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- 200×10^6 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	Cyropreserved product in PlasmaLyte-A + 1% HSA and CS10 stored in LN ₂ 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 7



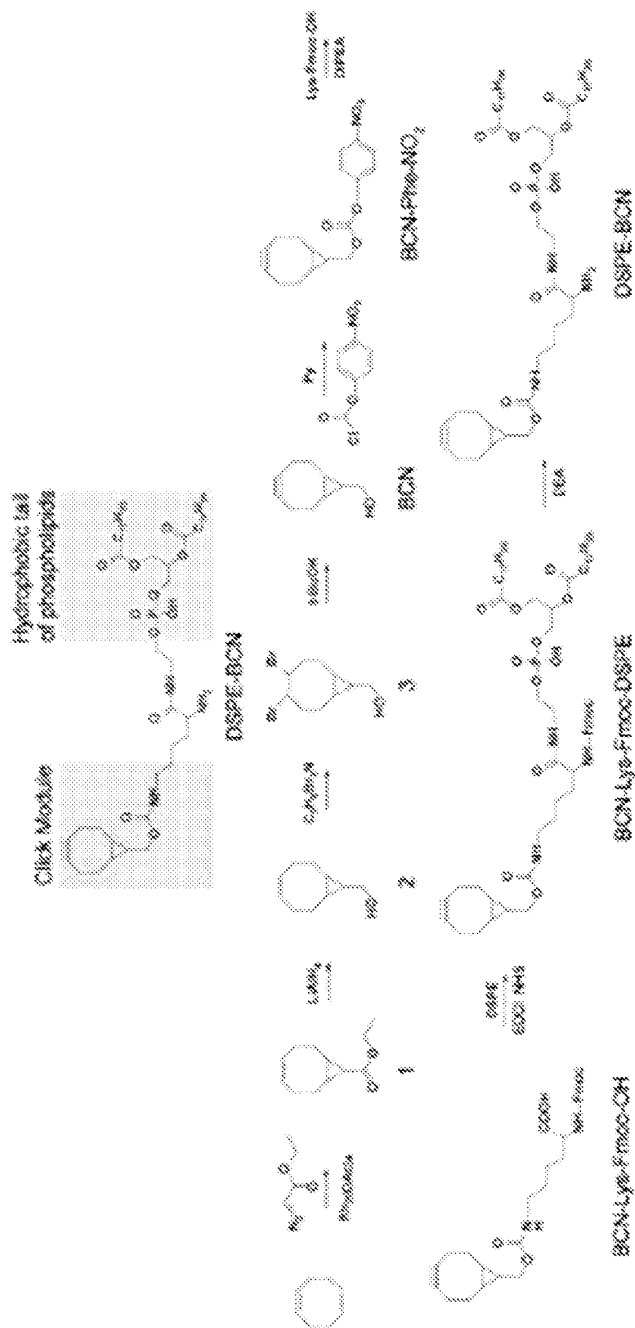


Figure 8A



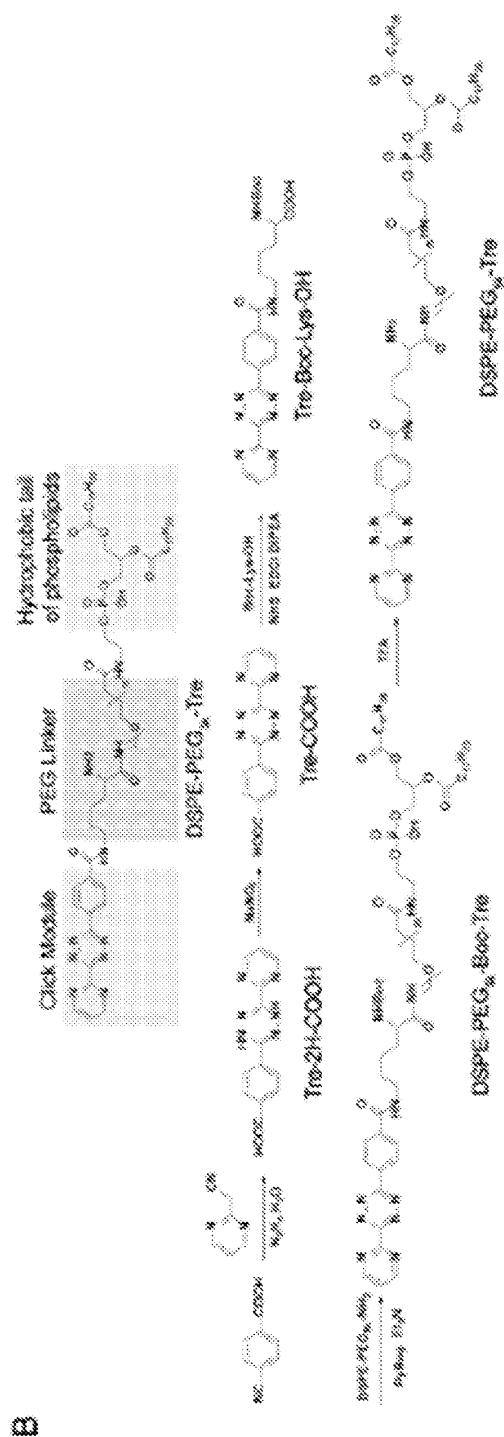


Figure 8B

Figure 9

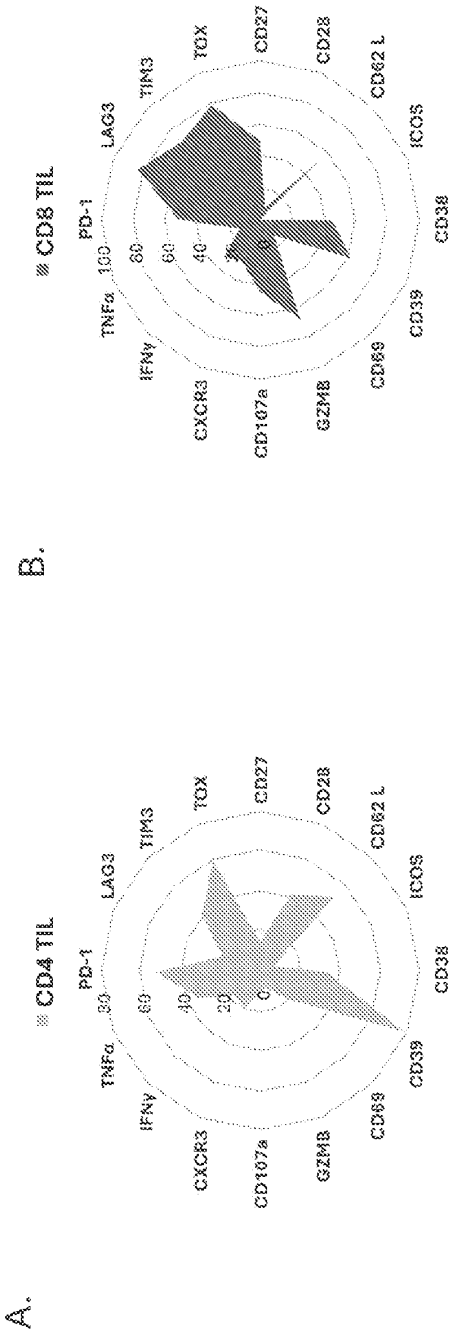


Figure 10

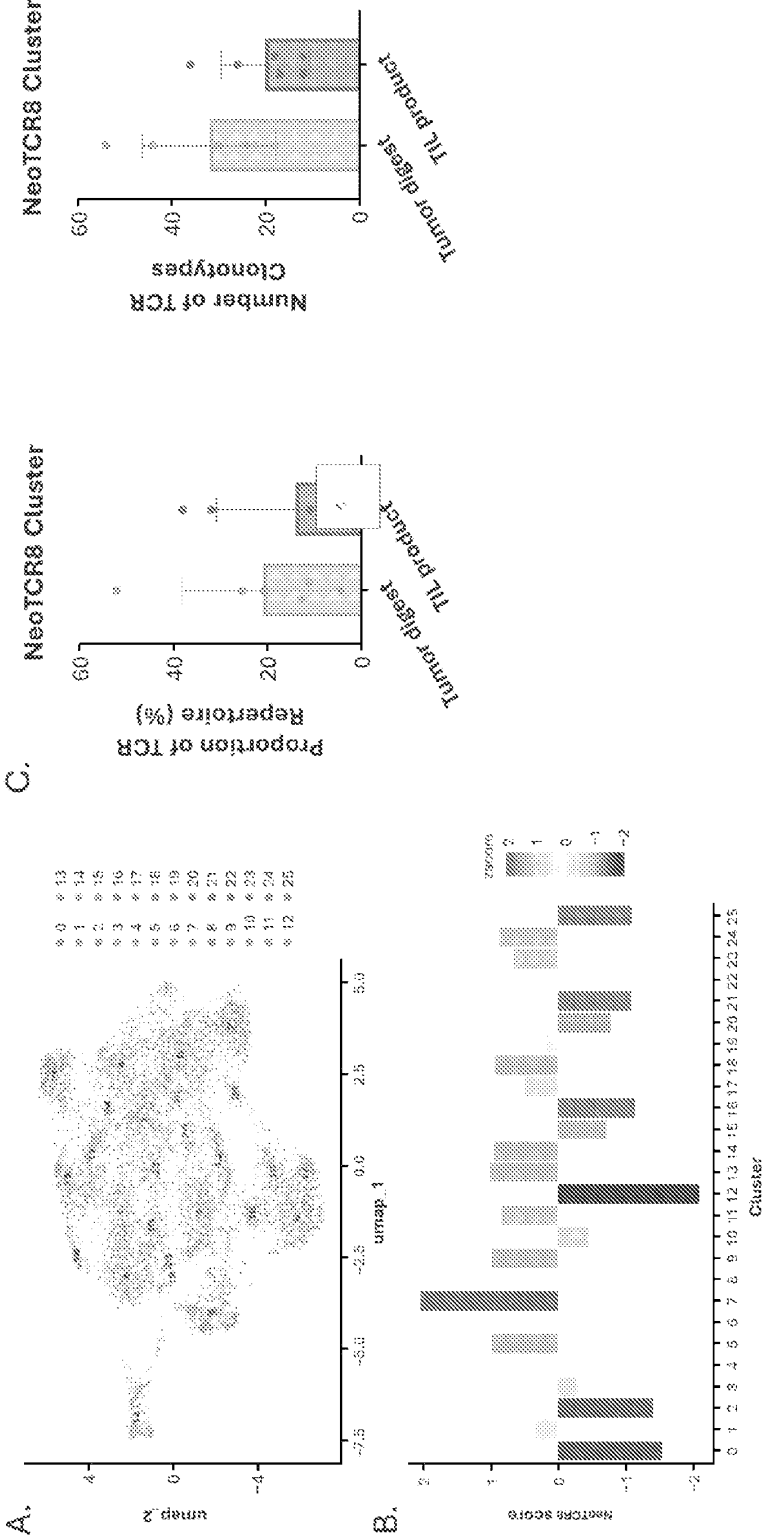


Figure 11

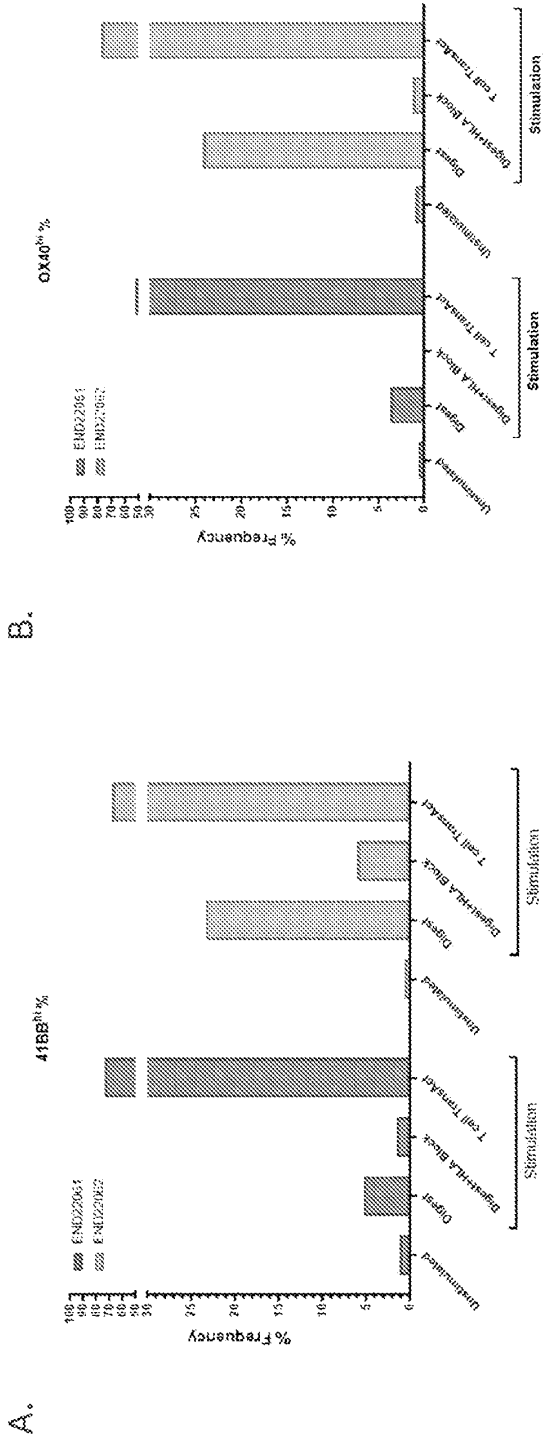


Figure 12

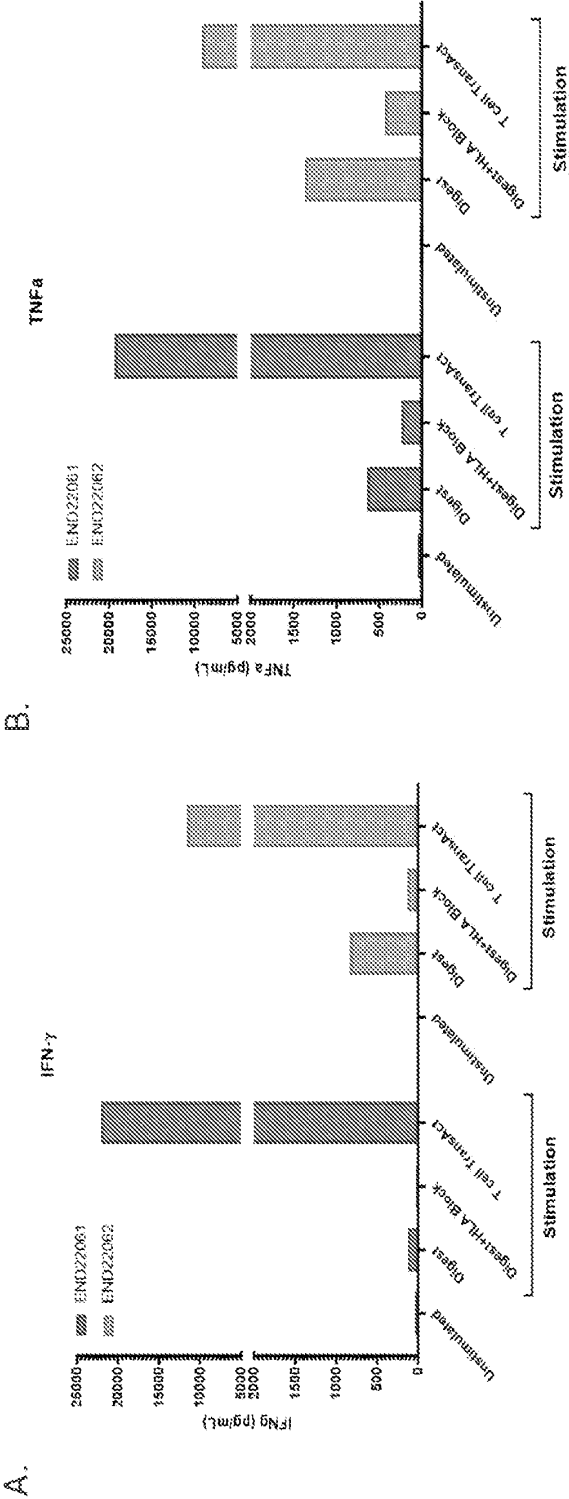


Figure 13

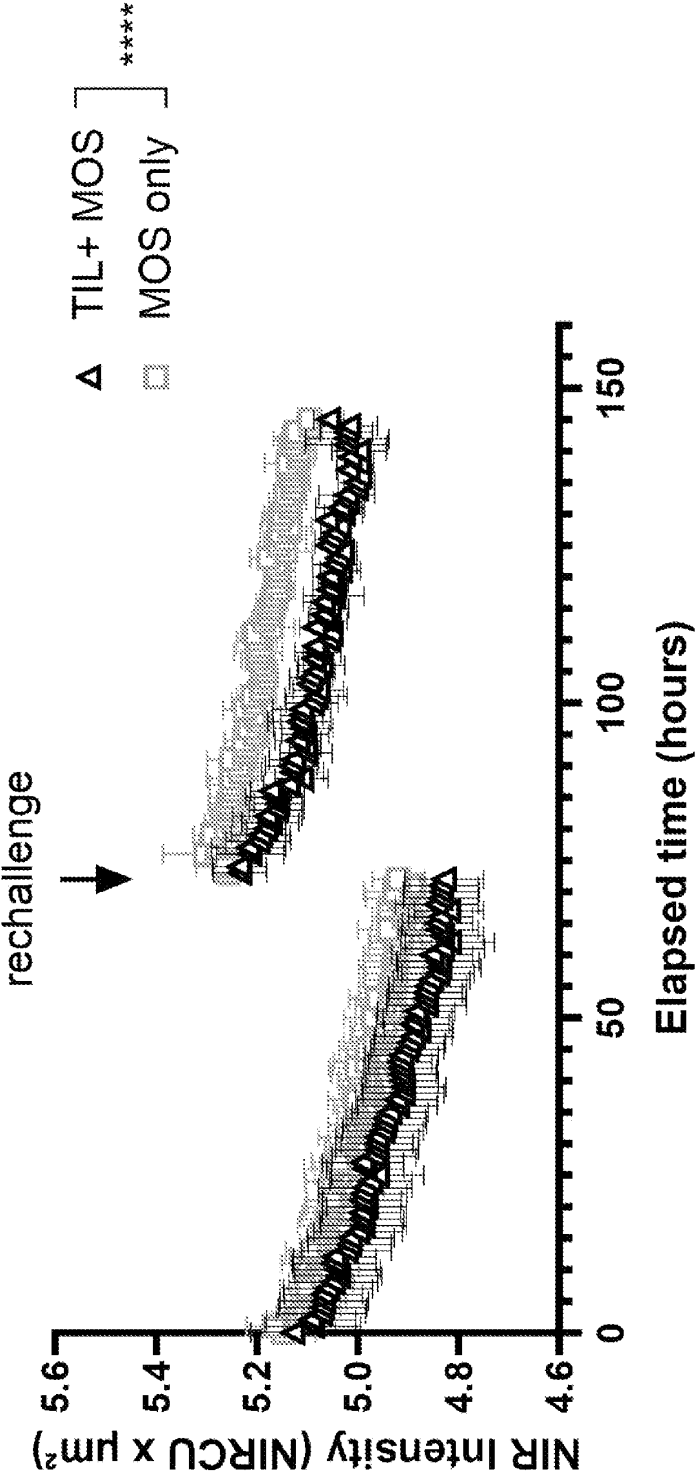


Figure 14

