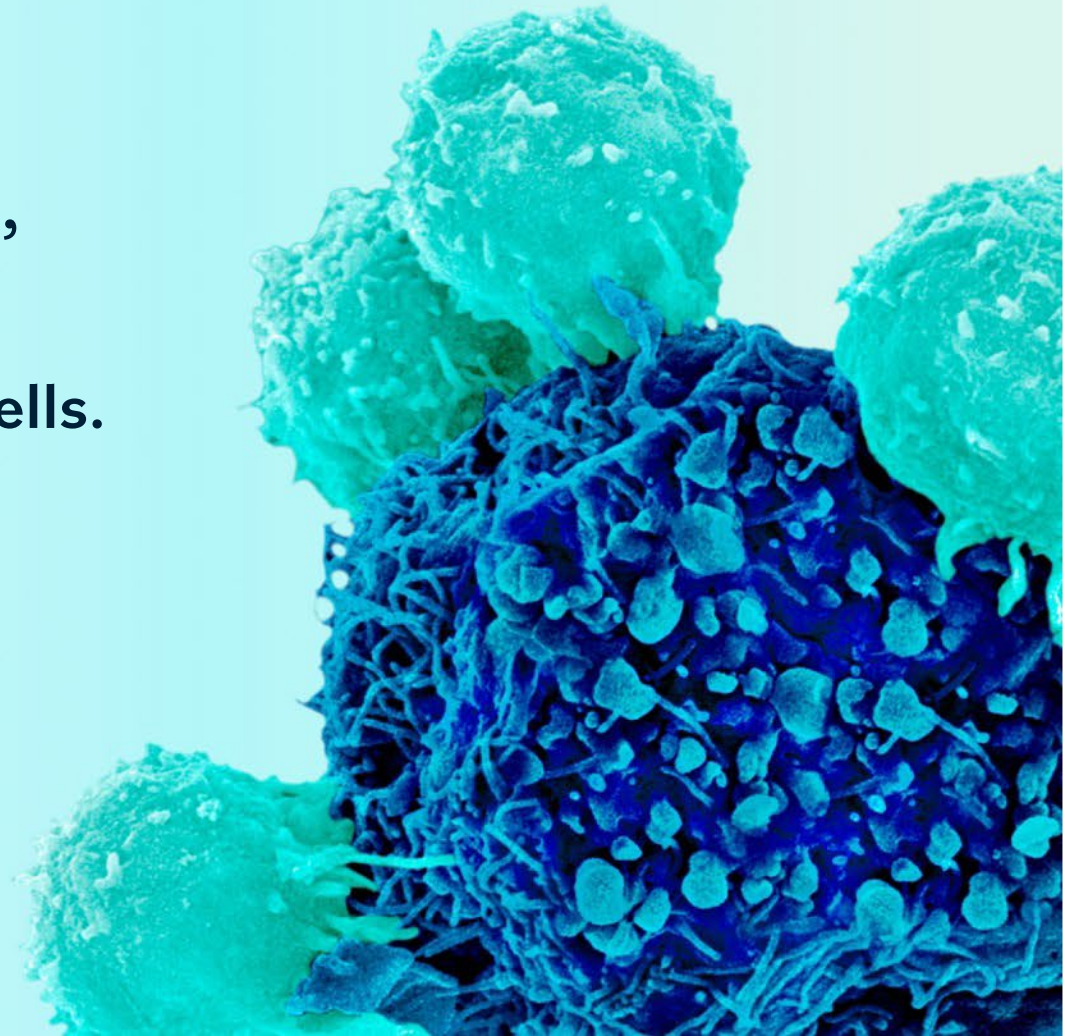
Alloplex Biotherapeutics

July 2026

The ENLYST™ immune cell training platform, a simple, robust and cost-effective method for manufacturing SUPLEXA™ therapeutic cells.

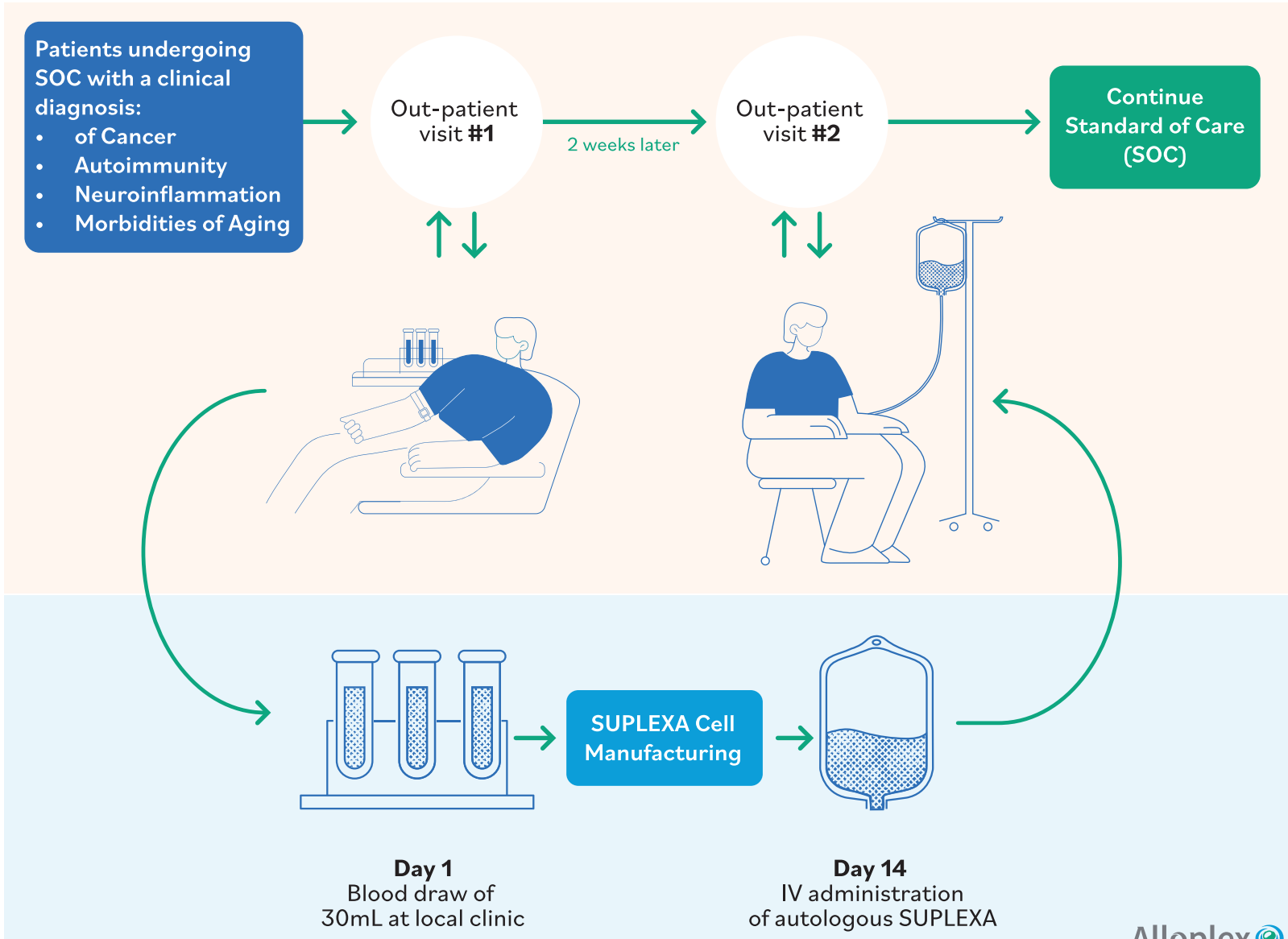
These uniquely activated, tissue-resident cells combine potent cytolytic activity with the expression of antigen-presenting properties to target oncology, autoimmunity, and chronic inflammatory conditions driven by senescent cells.



The patient experience of locally manufactured and delivered SUPLEXA treatment is only a 2-step process

Note: proprietary SUPLEXA cell manufacturing is protected by both patent and, more importantly, by trade secret, assuring long-lived protection of intellectual property.

- *Pristine safety profile* permits out-patient treatment as a single-agent or in combination with standards of care provided they are not toxic to immune cells.
- *Robust, efficient and cost-effective* manufacturing permits local manufacturing.
- *Simplicity* of the overall process combined with excellent clinical attributes supports broader use.
- *Affordability* – COGs are estimated to be ~$1,000 per 1B cells at scale and relate directly to patient access.



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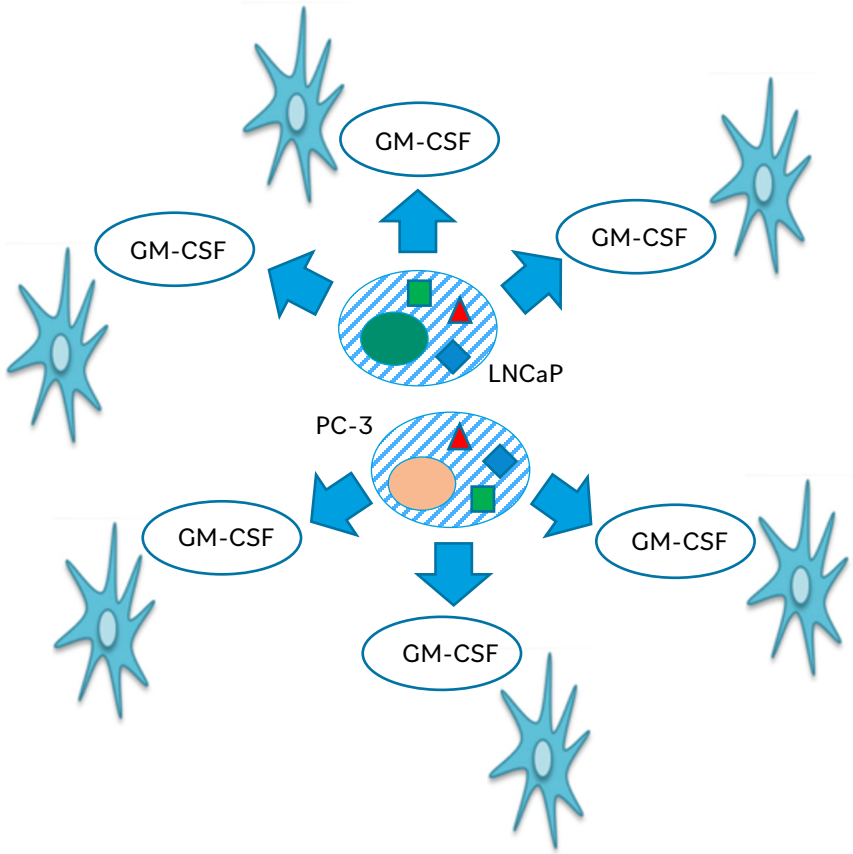
INSPIRATION

Key event in the history of cell vaccination using tumor cell lines transfected with a single immunomodulator, GM-CSF, confirmed the ability to modulate the anti-tumor clinical immune responses

Company: *Cell Genesys (founded in 1988 by Raju Kucherlapati PhD, led by CEO - Stephen Sherwin, MD),* ***Asset:*** *GVAX,*
Outcome: *failed in Phase 3 in 2008 when tested in combination with chemotherapy*



Phase 2 clinical data demonstrated measurable benefit

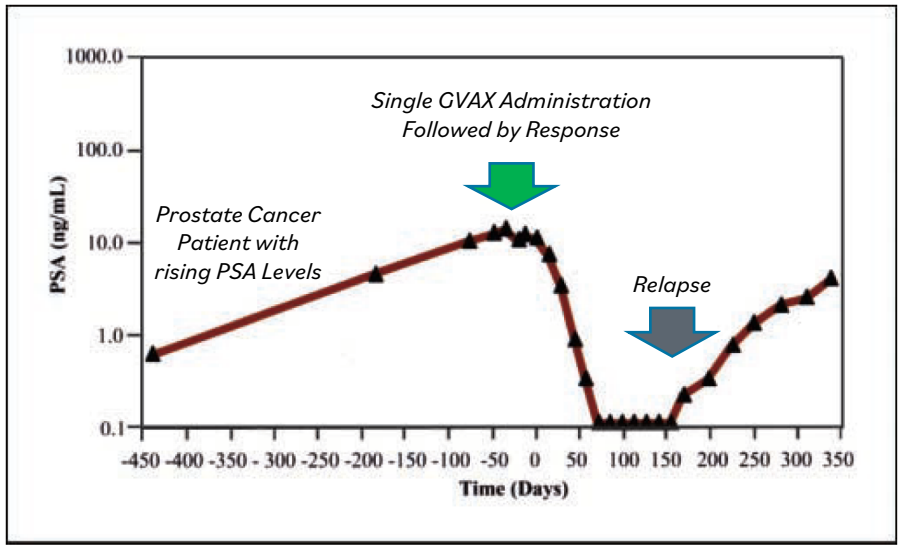


Fig. 1. Serum PSA over time in a patient in the radiologic group on the high dose of immunotherapy (patient G03-018-804SS).

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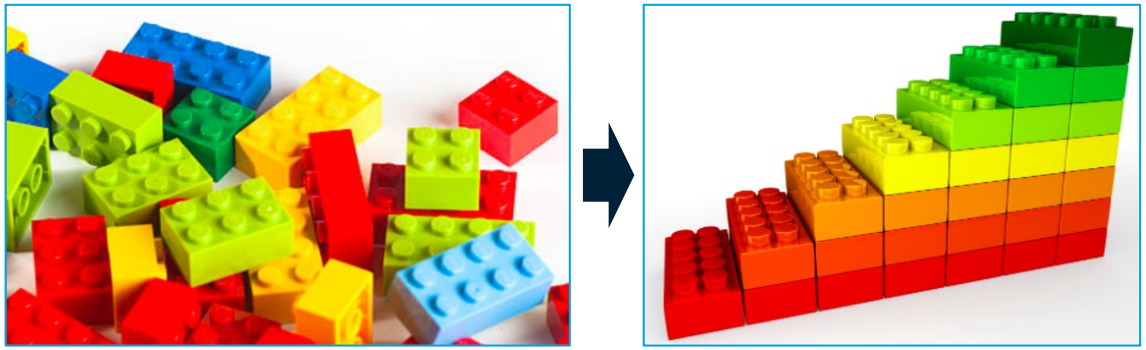
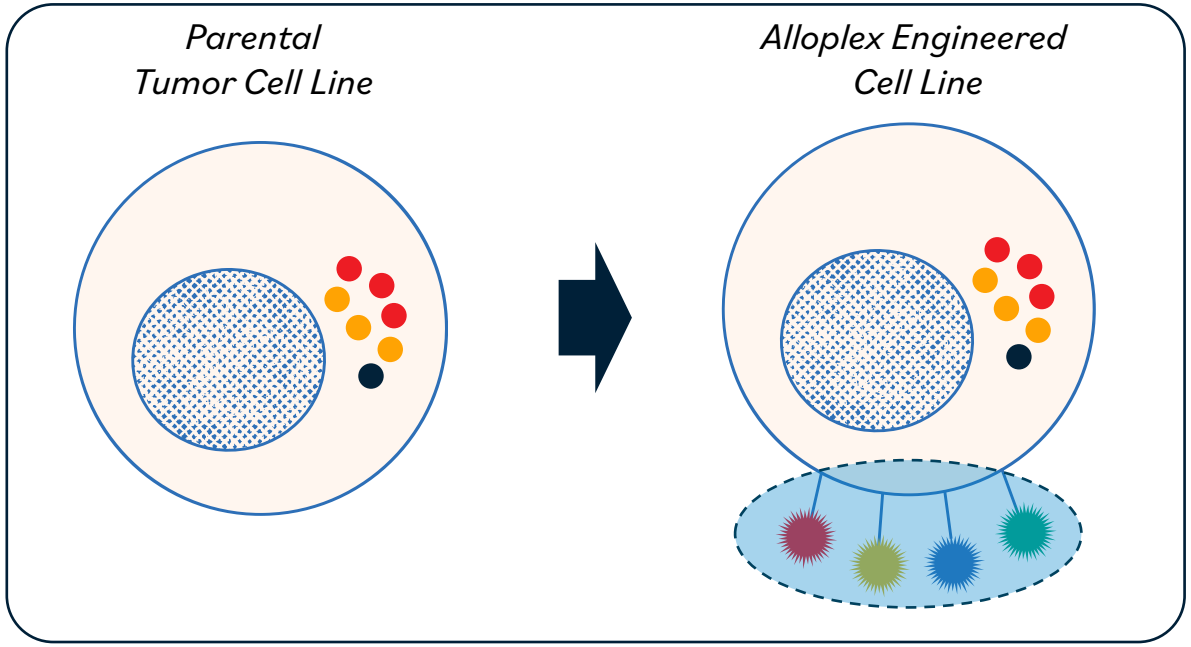
The Alloplex Concept

(multiplex engineering of an allogeneic tumor cell line)

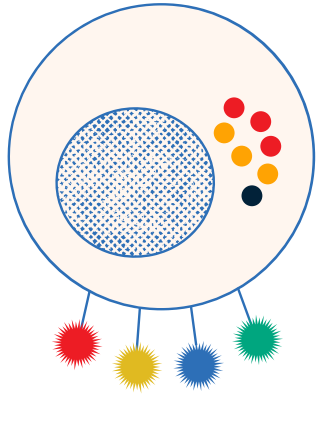
- *Systematic examination of the immunomodulator combinatorial space to reveal different activities and synergies between receptor signaling pathways.*
- Employ an allogeneic tumor cell line that may already possess a *broad array of antigens.*
- Engineered an optimal combination of immunomodulatory proteins to serve as *precision adjuvants*.
- Designed to *engage a wide range of native immune receptors* on various cellular elements, each known to have some contribution in driving effective anti-tumor responses.





The ENLYST-mediated immune cell training platform is key to SUPLEXA manufacturing

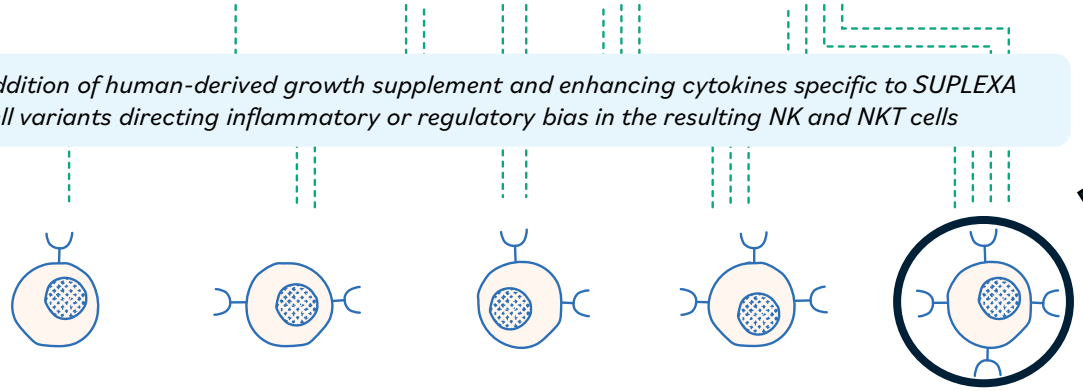
Proprietary ENLYST Induction Reagent protected by patents and trade secret



Immunomodulatry Ligands

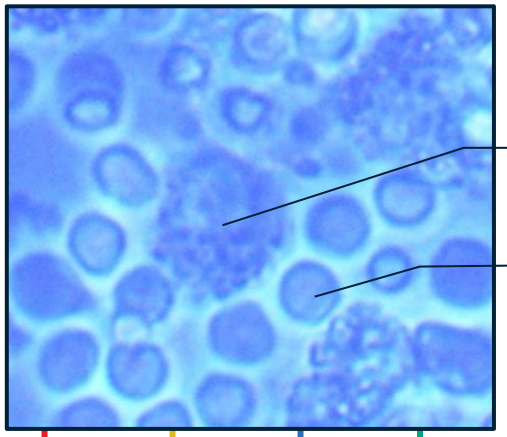
ENLYST Induction Reagent (IR)

Addition of human-derived growth supplement and enhancing cytokines specific to SUPLEXA cell variants directing inflammatory or regulatory bias in the resulting NK and NKT cells



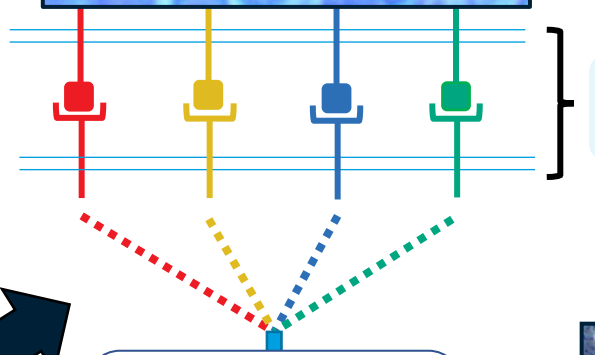
Naturally Occurring Immunomodulatory *Receptors* on PBMC. White Blood Cells.

Note that multiple immune cell subtypes, naturally present in PBMCs, each express a unique array of receptors.



ENLYST Induction Reagent

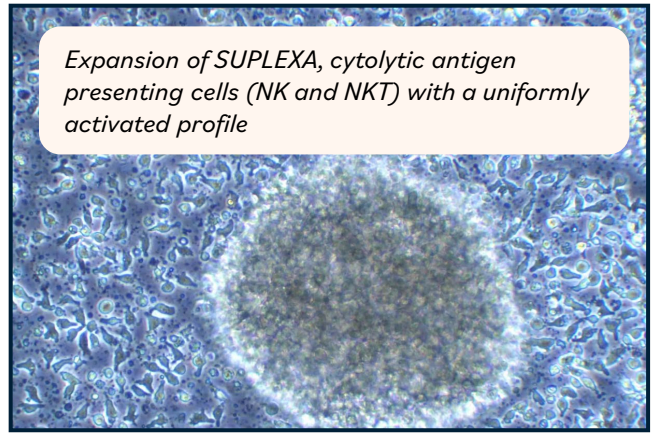
Resting white blood cells



Receptor-Ligand Pairs form at the immune synapse

Integration of receptor signaling

A Singular Biologic Response
- Proliferation
- Differentiation
- Cytokine Production
- Target cell killing capacity



Expansion of SUPLEXA, cytolytic antigen presenting cells (NK and NKT) with a uniformly activated profile

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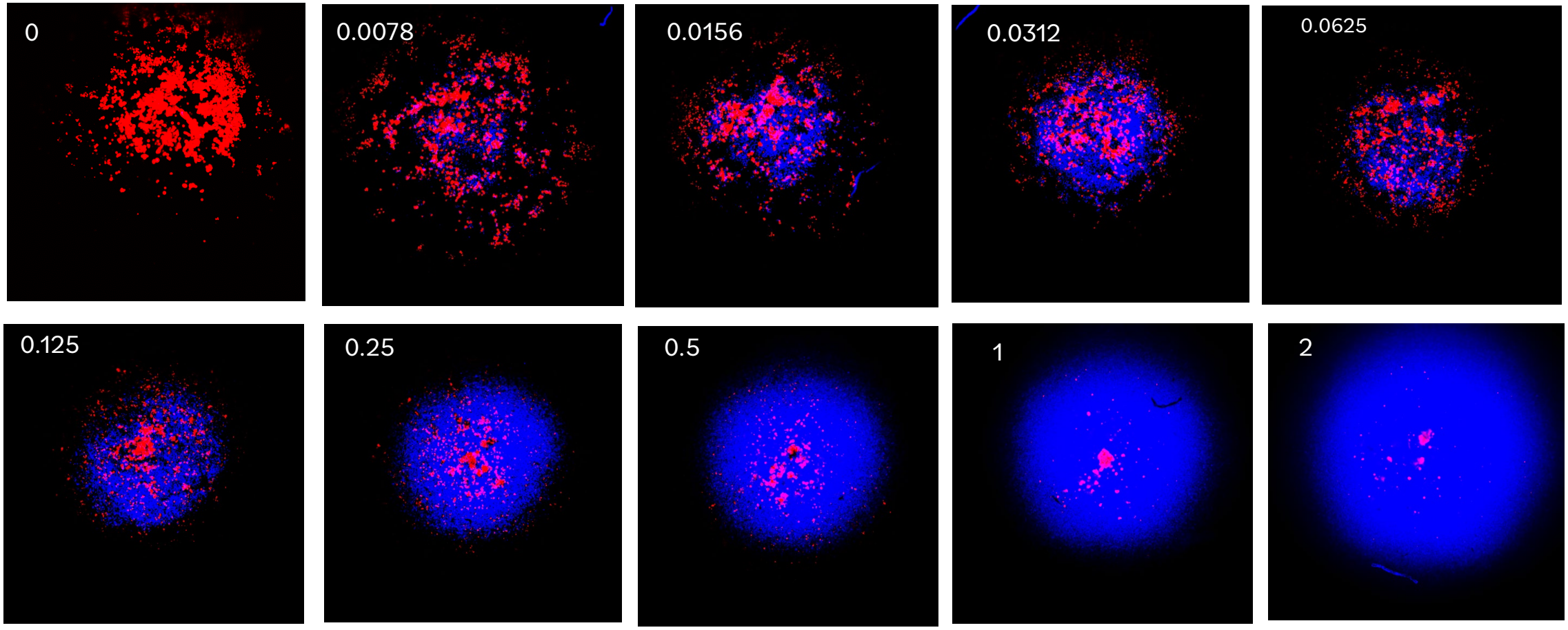
NSCLC PDX Organoid Data

CTG-3651 SUPLEXA Cells 24h treatment; similar results observed for a CRC PDX model)



Live PDX Tumor Cells

Live SUPLEXA Cells

- Representative images from Day 4 of the assay (Images after 24 hours of co-culture)
- Representative images from each of the nine cell concentrations tested are shown here with cell number (in millions) in the top-left corner at 4x magnification. Contrast has been adjusted to optimally depict representative images at higher cell doses, but uniform settings were used throughout for analysis.

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SUPLEXA cells act by multiple mechanisms at discrete steps in the cancer-immunity cycle

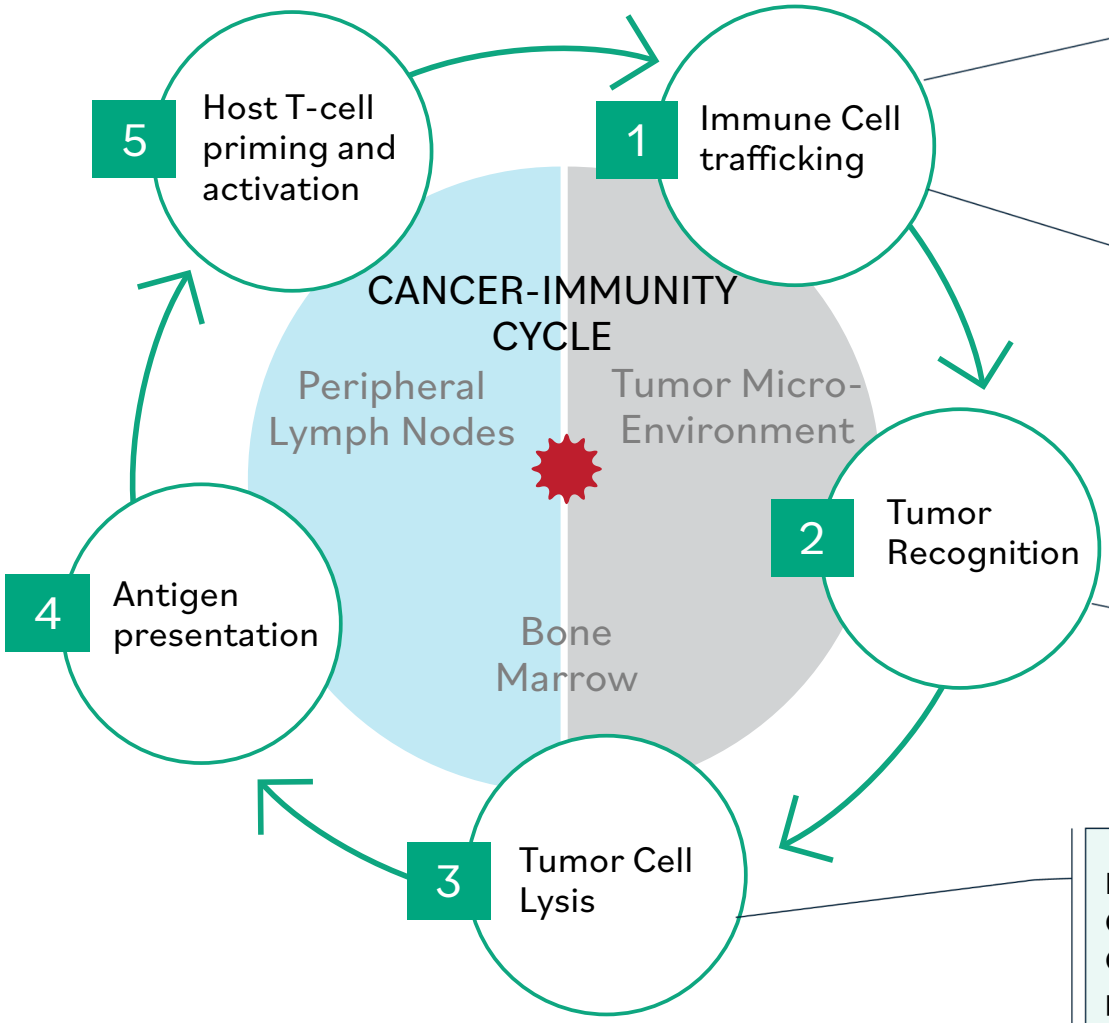
Costimulatory molecules for activating T cells (e.g., CD80 and CD86)

Antigen presentation (via HLA Class I and Class II molecules)

Antigen capture and processing (via scavenger molecules and proteases)

APC Function Requires HLA Class II matching

- Autologous cells are matched at all 3 loci; namely DR, DP and DQ



Adhesion molecule like CD62L required for exiting the vasculature

Chemokine receptors, such as CXCR4 and CX3CR1, are required for trafficking to TME, BM and lymph nodes

Activating molecule like NKG2D recognizes ubiquitous tumor antigens

Pore forming, cytolytic proteins like Granzymes A, Granzyme B, Perforin and Granulysin, cytokines like IFNg and membrane proteins like TRAIL and FAS Ligand

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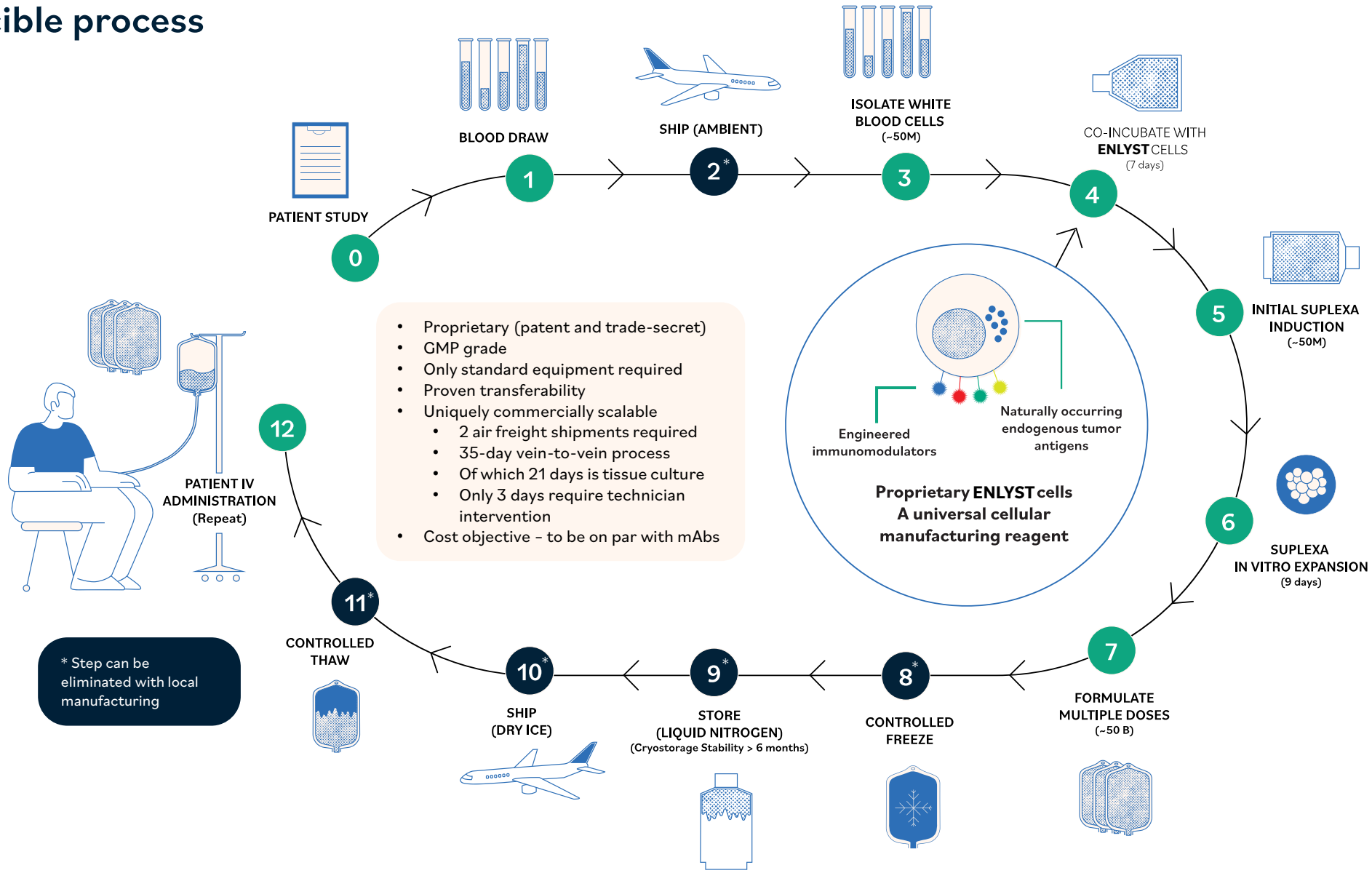
SUPLEXA are made by a clinically validated individualized, robust and reproducible process

Note: Alloplex has overcome many of the issues associated with Individualized manufacturing and therapeutic implementation.

- No leukapheresis,
  - just venipuncture and PBMC isolation
- No cell selection
- No genetic engineering
- No chemo preconditioning for lymphodepletion
- No clinical cytokine support required
- Multiple doses possible



- Proprietary (patent and trade-secret)
- GMP grade
- Only standard equipment required
- Proven transferability
- Uniquely commercially scalable
  - 2 air freight shipments required
  - 35-day vein-to-vein process
  - Of which 21 days is tissue culture
  - Only 3 days require technician intervention
- Cost objective – to be on par with mAbs

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SUPLEXA Therapeutic Cells

The first cell therapy candidate to emerge from the ENLYST immune cell training platform has successfully completed a FIH Phase 1 study in solid tumor patients

- Lead program - autologous (self), non-engineered, PBMC-derived option.
  - Unbiased approach requiring no cell selection.
  - Avoids the introduction of immunogenicity through expression of a foreign protein which could be recognized by the host and negatively impact cell persistence and durability.
  - Follows an established regulatory paradigm.

- Manufacturing - Requires only ~50 mL of whole blood and 3-week culture period
  - Highly scalable manufacturing with multiple infusions made from a single manufacturing batch.

- Uniquely activated immune cell product comprised predominantly of NK- and T- lineage cells.
  - High levels of HLA Class II, T cell costimulators, cytolytic proteins, activation proteins, cytokines and chemokines with their associated receptors.
  - Notably, it is devoid of exhaustion markers such as PD-1 and NKG2A checkpoints

- *Single-agent Phase 1 study in metastatic solid tumor patients achieved all prespecified endpoints*
  - Entry Criteria - Patients had exhausted all standard options including chemo and checkpoint inhibitors.
    - No chemo preconditioning or supportive cytokines were used.
  - Safety – Pristine profile (only several transient Grade 1/2 adverse events).
  - Efficacy – activity in multiple solid tumor types with durability.
  - Exploratory - pharmacodynamic biomarkers identified in myeloid blood composition.

- Multiple potential mechanisms of activity have been identified for SUPLEXA cells.

Perspective on SUPLEXA cell number relative to host immune cell populations

Ex Vivo Manufacturing

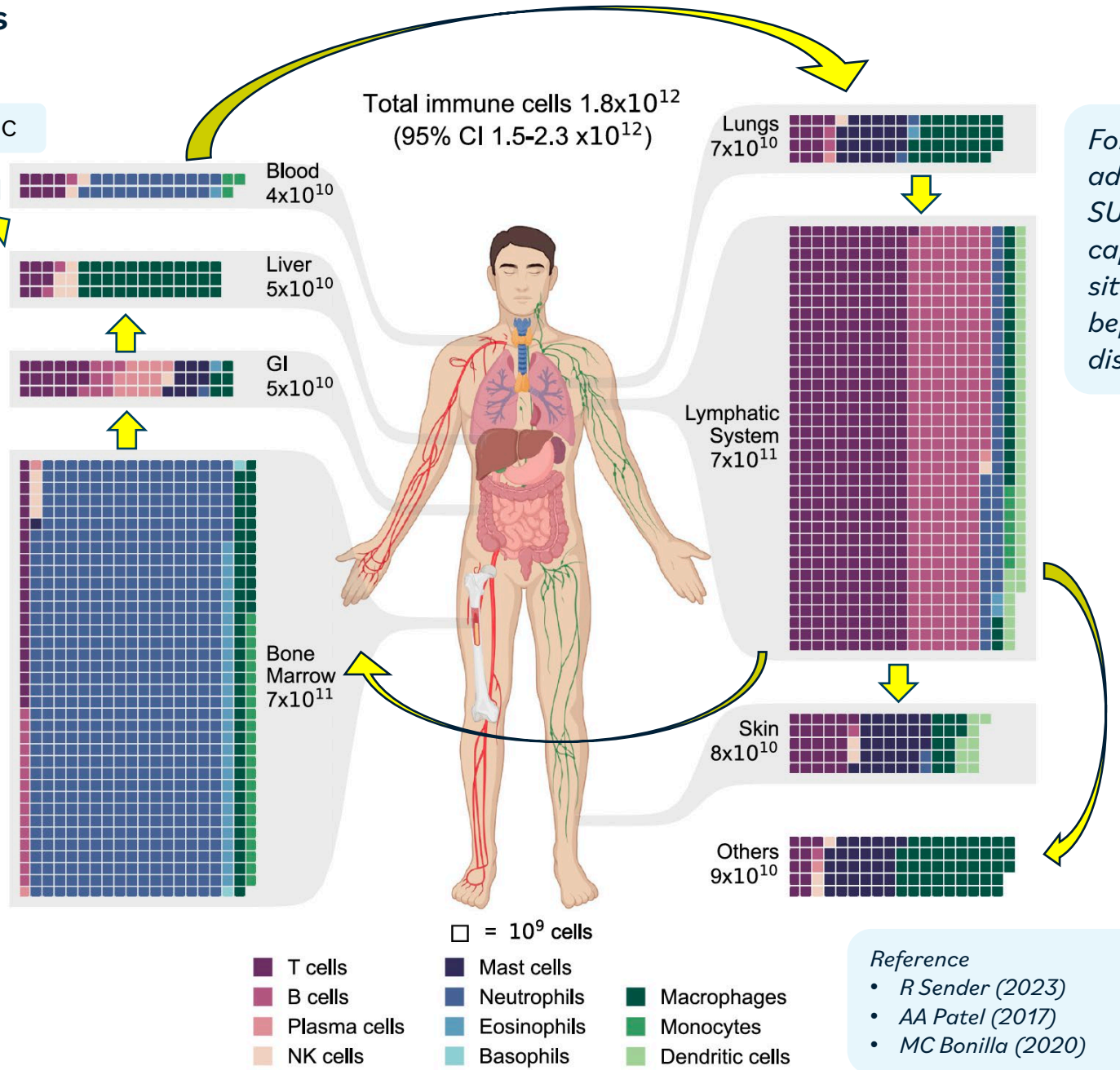
~50 M PBMC

SUPLEXA manufacturing

SUPLEXA dose (2 x 10 B cells)

(~3-5% of bone marrow cell number)

CXCR4 and CXCR3 chemokine receptor expression on SUPLEXA cells allow them to traffic to the bone marrow and lymph nodes



Following IV administration of SUPLEXA, the lung capillary bed is the first site of accumulation before further distribution

Tumor Microenvironment (Variable numbers of TILs)

Reference

- *R Sender (2023)*
- *AA Patel (2017)*
- *MC Bonilla (2020)*

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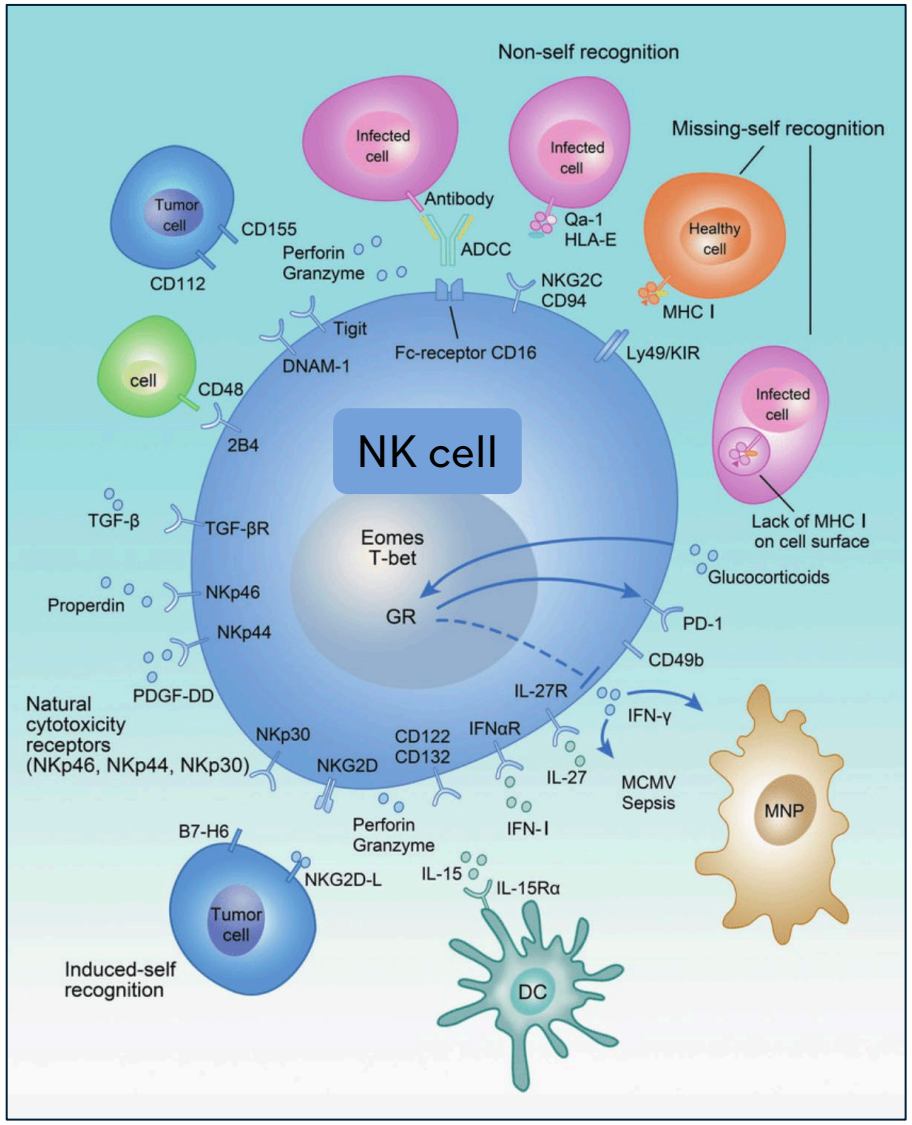
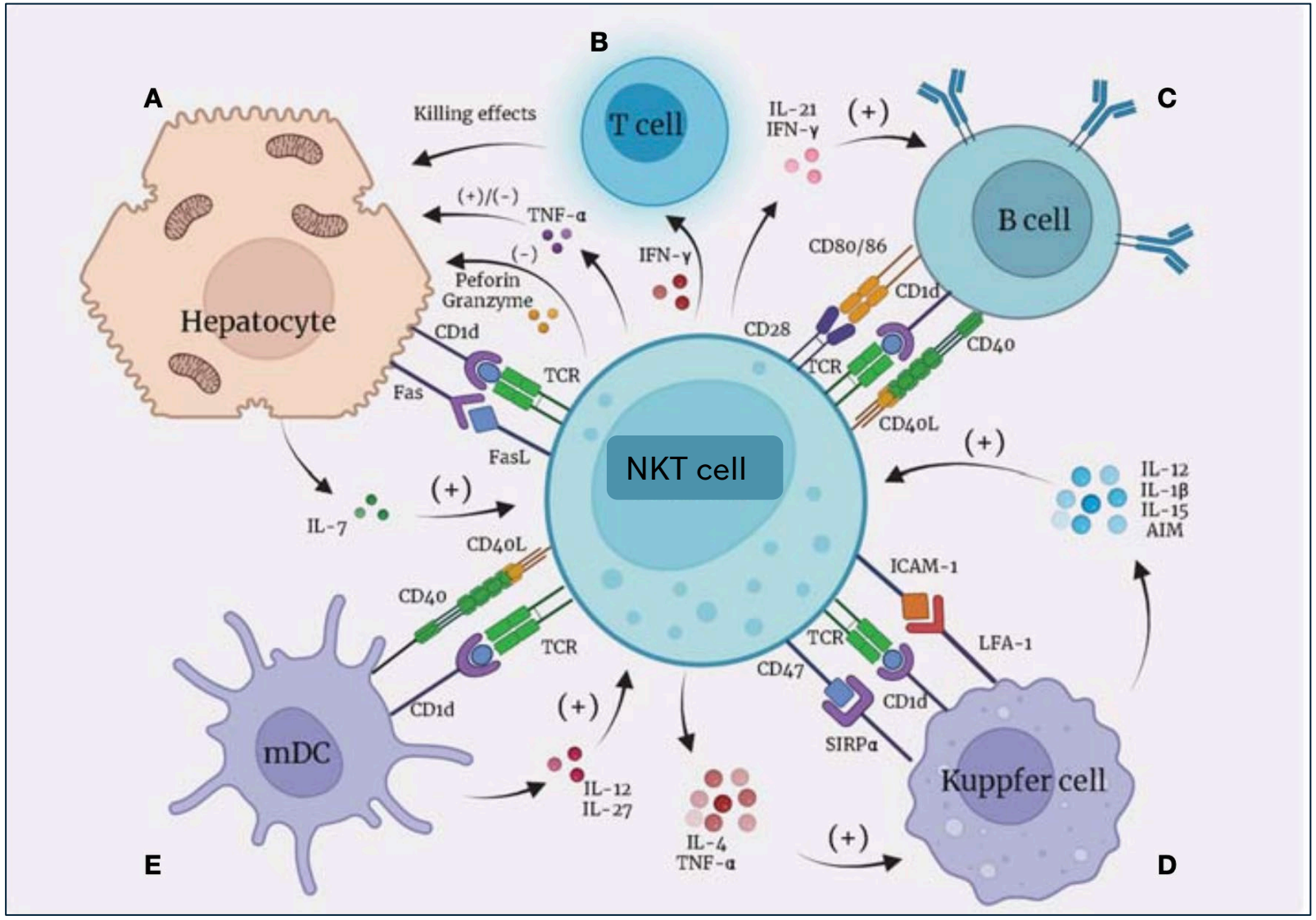
SUPLEXA cell therapy is comprised of autologous NK and NKT cells which are tissue resident cells of the innate immune system with broad immunoregulatory features





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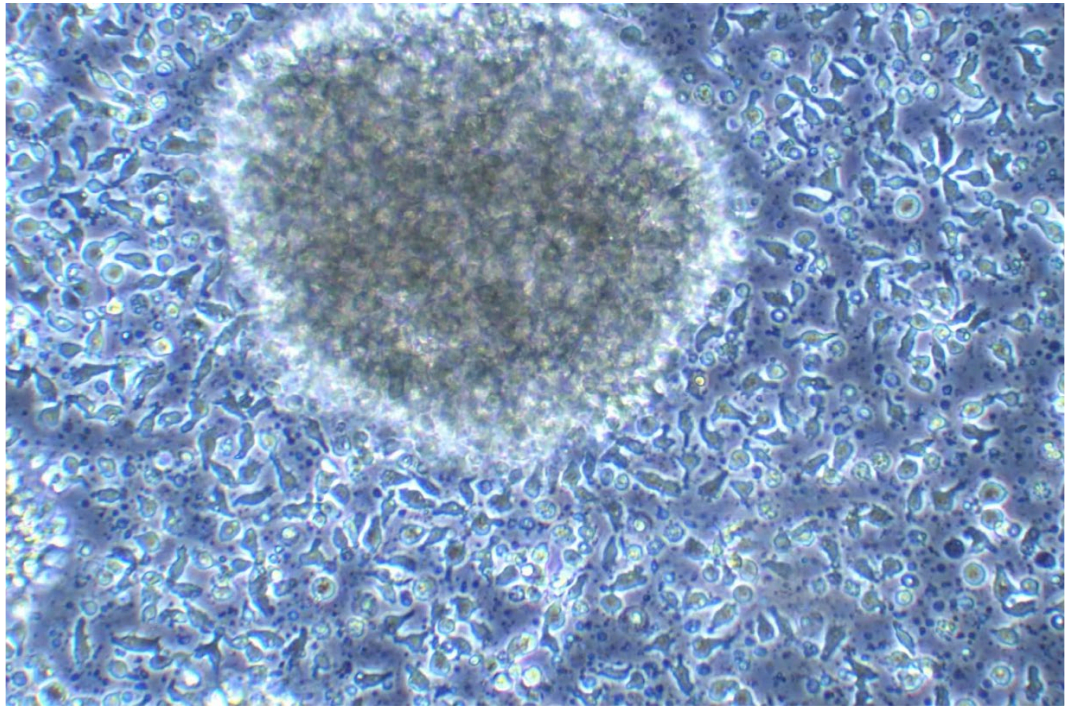
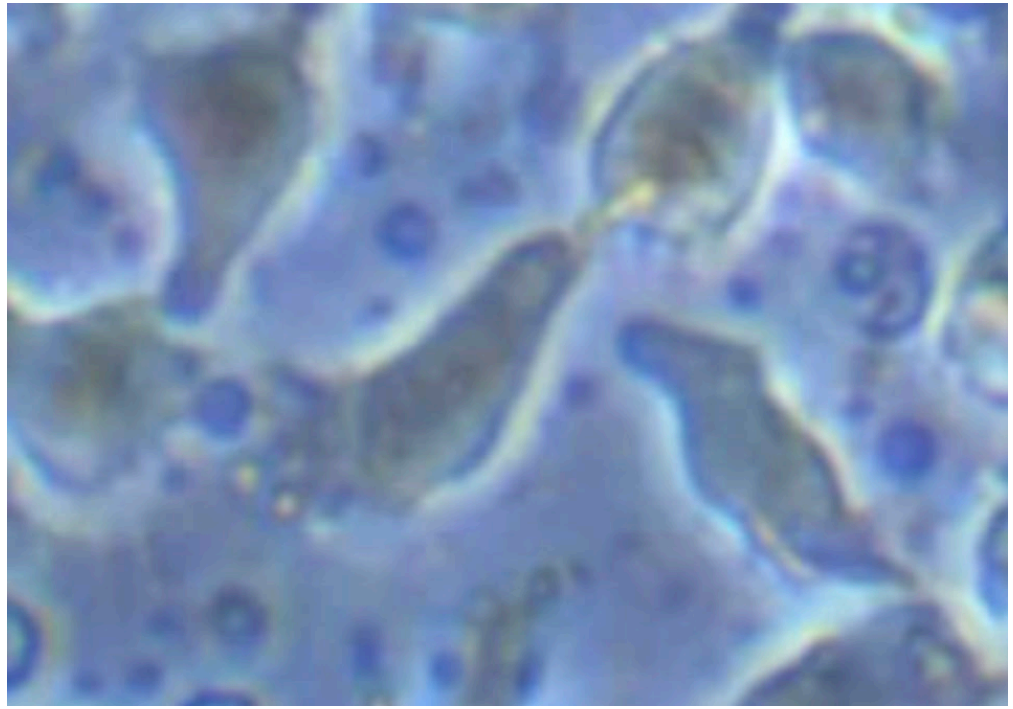
SUPLEXA Therapeutic Cells

Manufactured *ex vivo* from patient PBMCs using the ENLYST immune cell training platform, yield an autologous, non-engineered therapy comprised of activated NK and NKT innate immune cells.





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