ThermoFisher
SCIENTIFIC

Eliminate serum to gain control of your T cell research – New xenofree serum replacement

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Senior Manager, Product Development

Cell Therapy Systems (CTS™) Product Portfolio

Thermo Fisher Scientific

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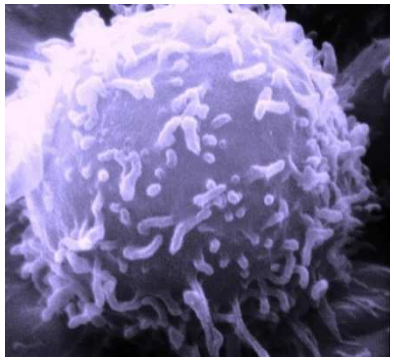
T-Cells Participate in a Variety of Cell Mediated Immune Reactions

What are T-Cells?



- T cells are one type of white blood cells
- T cells can help kill or directly kill “invaders”
- There are multiple types of T-cells
  “Helper" T-cells, “Killer" T-cells, Regulatory T-cells,

What are the functions of T-Cells?

- T cells can destroy cells infected by viruses, graft cells, and other altered cells, such as cancerous (e.g. Lymphoma)
  - “Helper" T-cells - stimulate the B cells and help killer cells develop.
  - “Killer" T-cells - kill cells that are altered
  - Regulatory T-cells can suppress immune responses such as autoimmune responses and graft rejection
- T cells also secrete cytokines
- Interact with antigen presenting cells and induce maturation

T Cells Used in Therapy

• Gene modified T cells

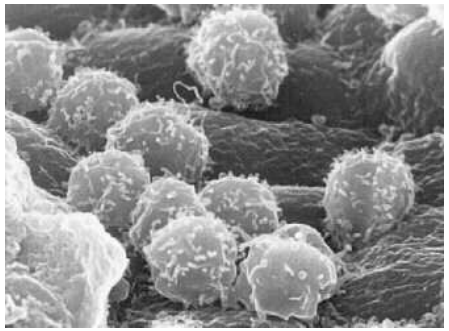
Cells that have a novel receptor placed on the surface of the cell in addition to the native TCR (CAR) or an engineered receptor to give it an enhanced affinity to the antigen (eTCR)

CAR (chimeric antigen receptor) - T cells isolated from a patient's blood are genetically engineered to produce special receptors on their surface called chimeric antigen receptors (CARs). CARs are proteins that allow the T cells to recognize a specific protein (antigen) on tumor cells. These engineered CAR T cells are then grown in the laboratory until they number in the billions and infused back into the patient to target specific antigens such as those on the surface of cancer cells.

http://www.cancer.gov/cancertopics/research-updates/2013/CAR-T-Cells

•Tumor Infiltrating Lymphocytes (TILs)

Cells pulled from a tumor with specific reactivity to a cancer antigen and expanded ex-vivo



• Antigen specific T cells

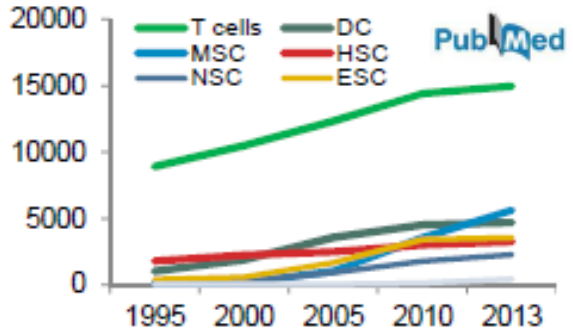
Cells exposed to antigen exogenously to be expanded and reinfused

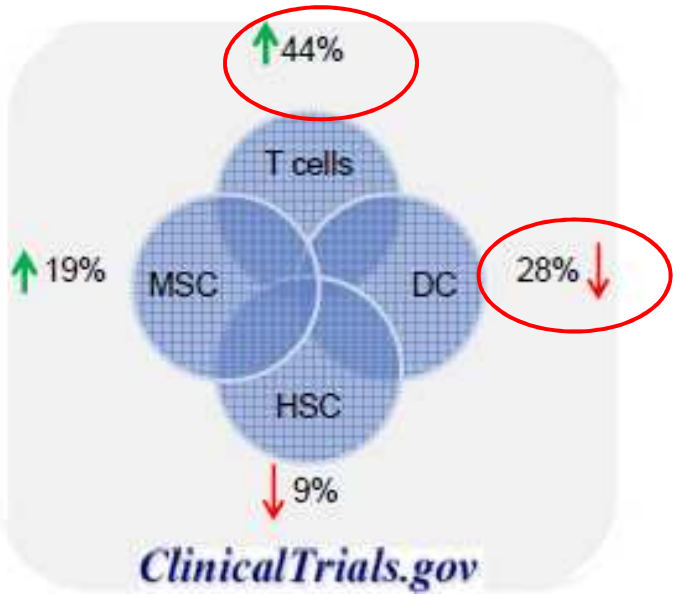
• Regulatory T cells

Cells that suppress the classic immune response and are used for autoimmune disease

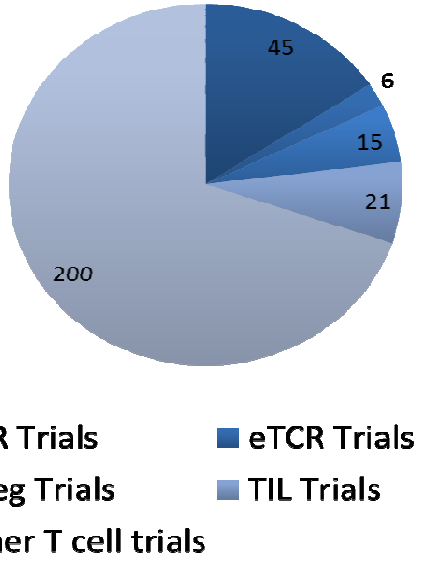
Immunotherapy Market Trends

Publication Trends





T Cell Clinical Trials



Area of Academic and Industrial Research Focus

NIH
University of Pennsylvania
City of Hope
NCSF
Fred Hutch Cancer Inst

NeoStem
Novartis
GSK
Juno
Cellectis
Bluebird
AdaptImmune
Kite Pharma

Motivating Factors in Cell Therapy

- Moving towards animal origin free

- Scale up/scale out

- Pharma partnering with academia and biotech

Supply Concerns Associated with Serum

"Serum Free is essential" for Cell manufacturing
Levine B.L. and C.H. June. 2013. Perspective: assembly line immunotherapy. Nature 498:S17.

"Current stocks and production rates of serum suitable for GMP manufacture may only be sufficient to support the production of one blockbuster cell therapy"
Brindley, Davie, Culme-Seymour, Mason, Smith & Rowley. Regen.Med (2012)7(1)

"would be interested in a defined serum free supplement that could replace serum in T Cell culture."
T Cell Survey May 2013: 100% (15/15) of respondents surveyed.

CTS™ Immune Cell SR Minimizes the Supply Risks Associated with Human Serum used in Your T Cell Culture

CTS™ Immune Cell SR is the first **defined**, **T-cell qualified** **xeno-free** replacement for human serum (for use in GMP T cell culture) that provides serum-based "results“ without the supply risk.

Specifications

Parameter	SPEC
Functional 4-day T Cell Assay	Acceptable vs. internal assay control
pH	>=7.0 to <=7.7
Osmolality	> =430 to < =500
Mycoplamsa testing (qPCR)	Negative
USP Sterility testing	Negative
Endotoxin testing (LAL)	>=0.0 to <=10.0
HBsAg, HIV1&2, HCV virus tesing*	Non reactive (Ab)

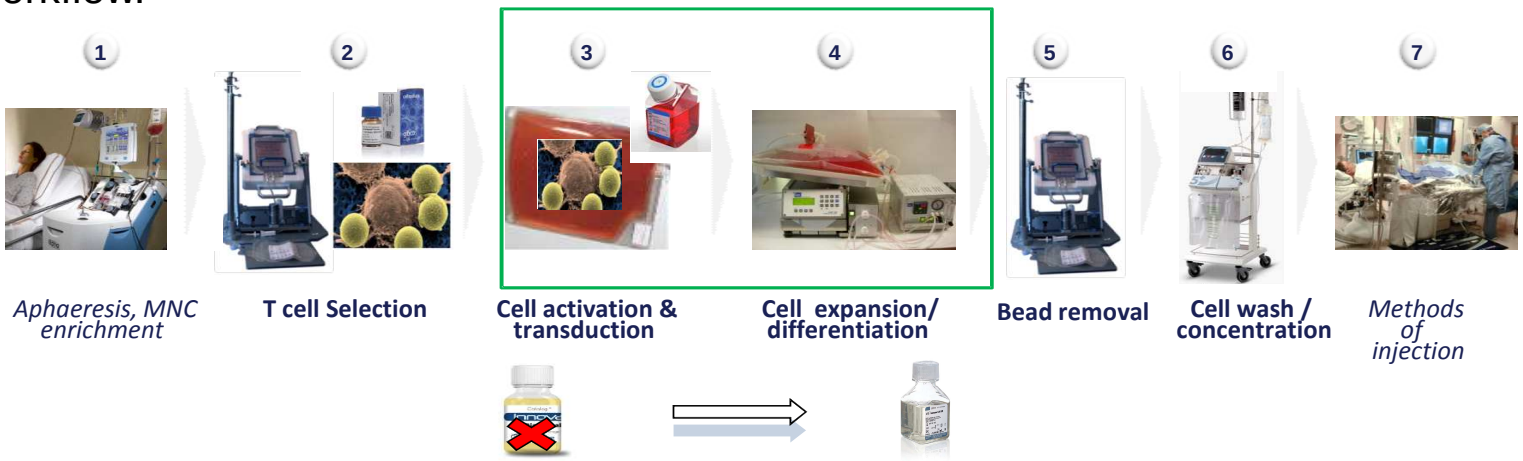
CTS™ Immune Cell SR is Ready for Your Commercial Success

- Formulation contains only human and chemically defined components with harmonized documentation (COO, COA, DMF)

- Each lot is pre-qualified in a functional primary T cell- assay to help ensure consistent performance

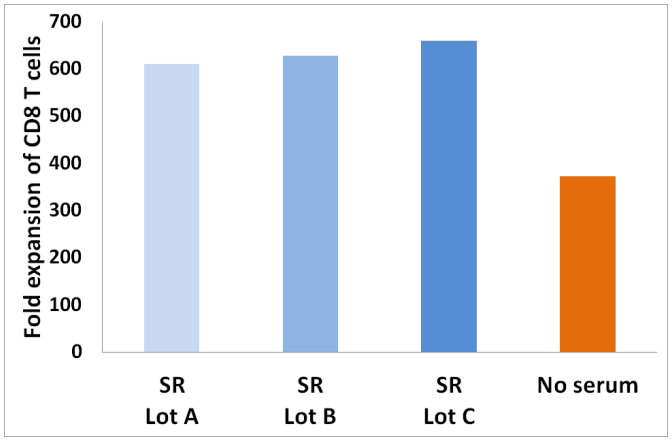
- Product is labeled as a Class I Invitro Diagnostic Medical Device with CE-IVD mark and is cGMP manufactured with a scalable process to ISO13485 standards. This product also meets USP 1043 Requirements for Ancillary Materials for Cell Gene and Tissue Engineered Products.

- Product can replace human serum across different media systems as a simple substitution into current workflow.

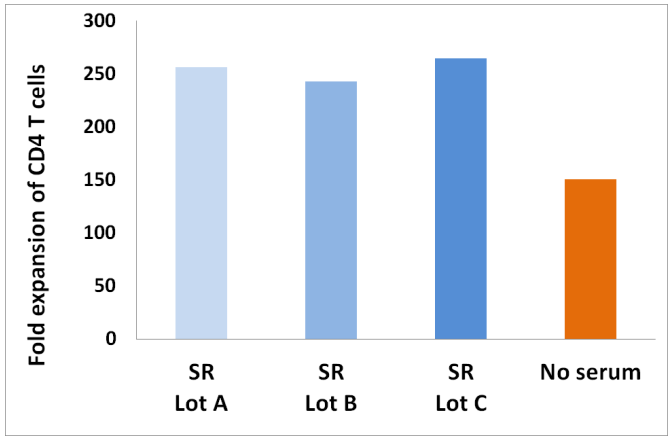


CTS™ Immune Cell SR Lots Perform Consistently and Support High Cell Viability

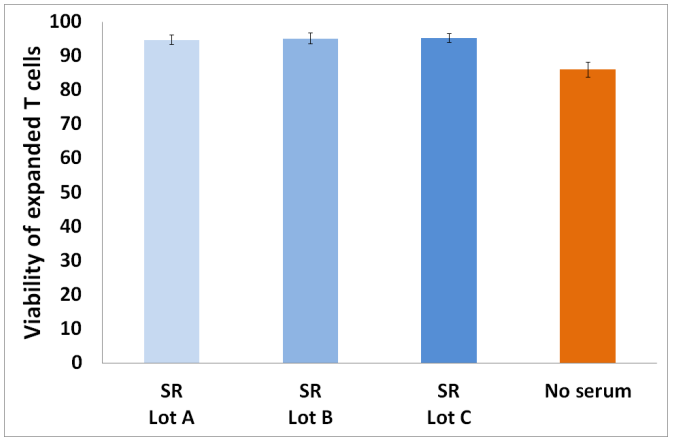
Consistency and high viability across 3 lots of CTS™



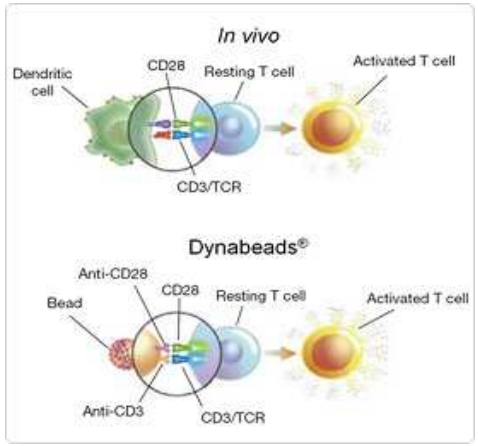
N=1 donor



T cells from PBMC were isolated and activated using CTS™ Dynabeads® CD3/CD28 and cultured in CTS™ OpTmizer™ T Cell SFM supplemented with 3 different lots of CTS™ Immune Cell SR (10%) or no serum.



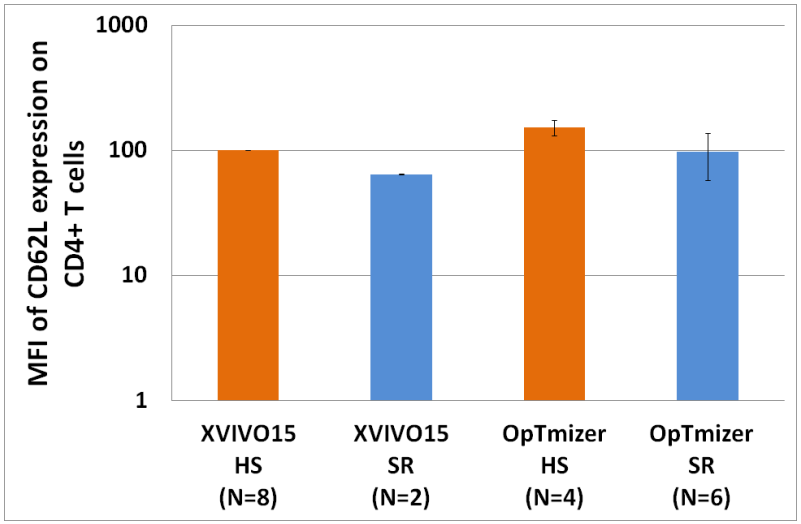
N=1 donor

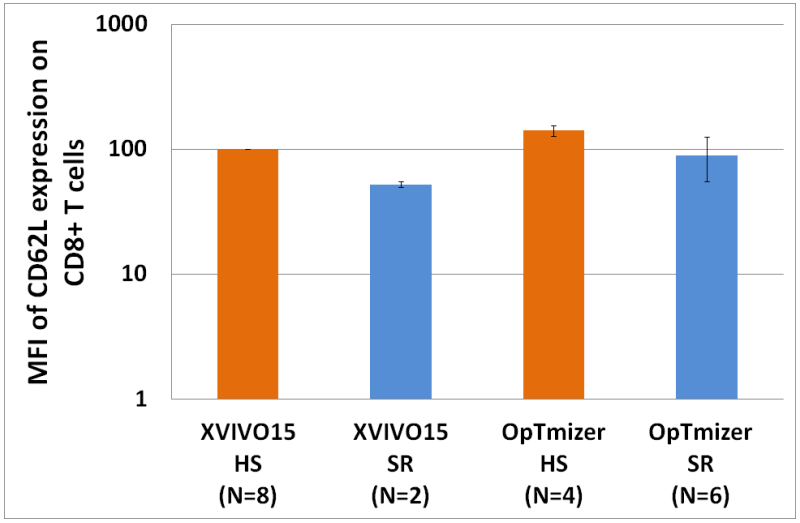


Activated T cells cultured in CTS™ OpTmizer™ T Cell SFM supplemented with 3 different lots of CTS™ Immune Cell SR maintain high cell viability

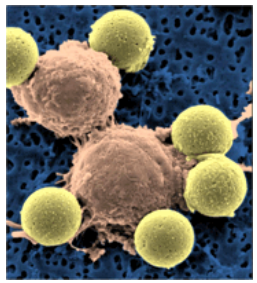
CTS™ Immune Cell SR Maintains CD62L Expression on CD4 and CD8 T Cells Similar to Human Serum

CTS™ Dynabeads® CD3/CD28 activated T cells cultured in CTS™ Immune Cell SR supplemented media or human AB serum expands T cells with T central memory phenotype



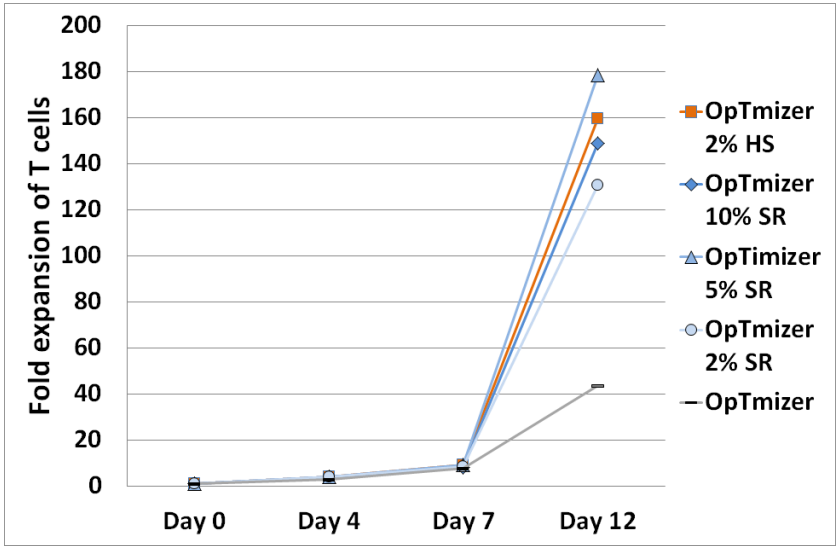


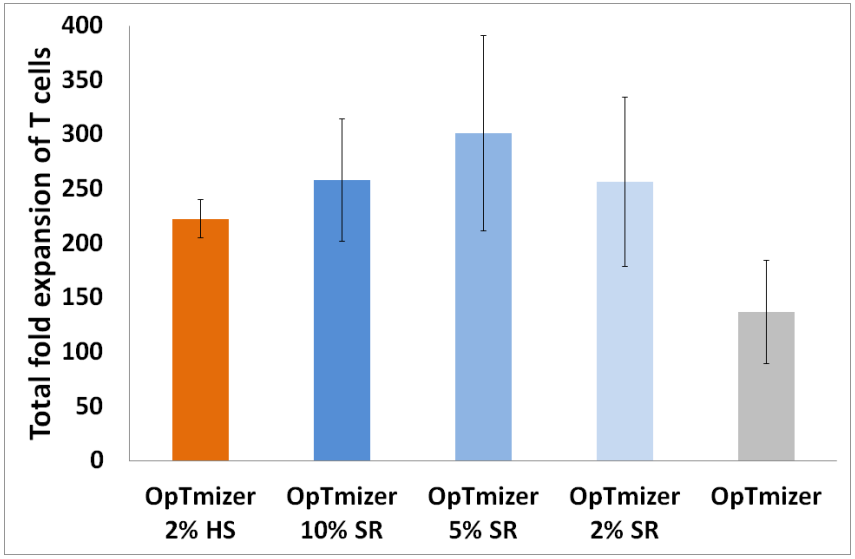
T cells from PBMC were isolated and activated using CTS™ Dynabeads CD3/CD28 and cultured in X- VIVO™ 15 or CTS™ OpTmizer™ T Cell SFM supplemented with 5% and 2% pooled human AB serum respectively or CTS™ Immune Cell SR (10%).



CTS™ Dynabeads CD3/CD28

CTS™ Immune Cell SR Supports Activated Polyclonal T Cell Expansion Similar to Human Serum

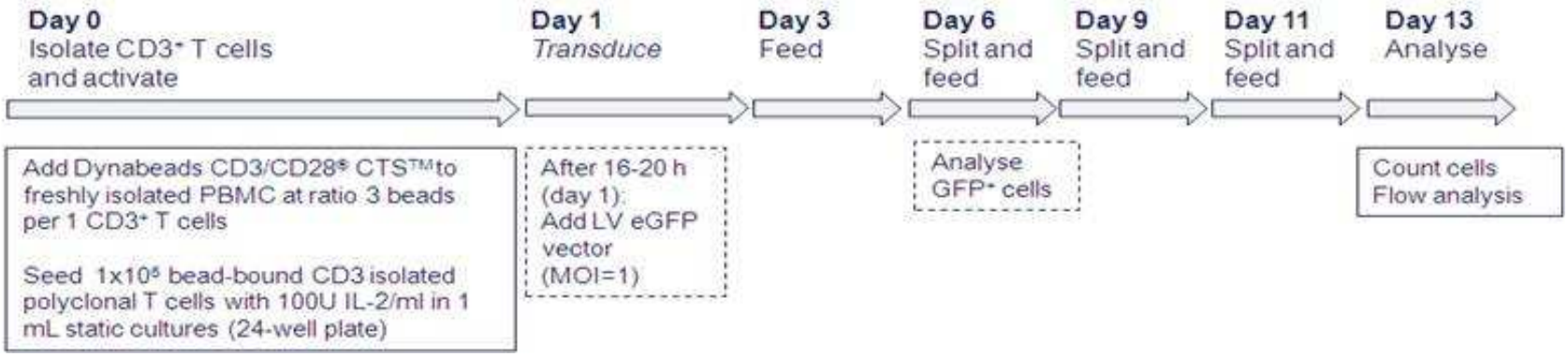


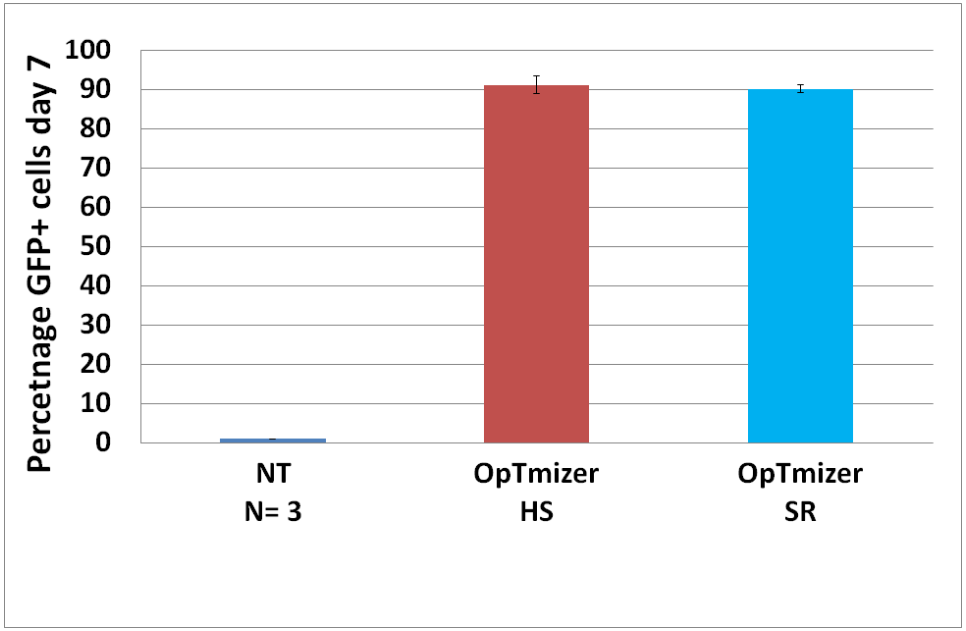


Growth Kinetics from one representative donor of T cells activated with Dynabeads® CD3/CD28 CTS™ in CTS™ OpTmizer™ T Cell Expansion SFM supplemented with CTS™ Immune Cell SR at 2%, 5% or 10% vs 2% Human AB serum.
N=1 blood donor.

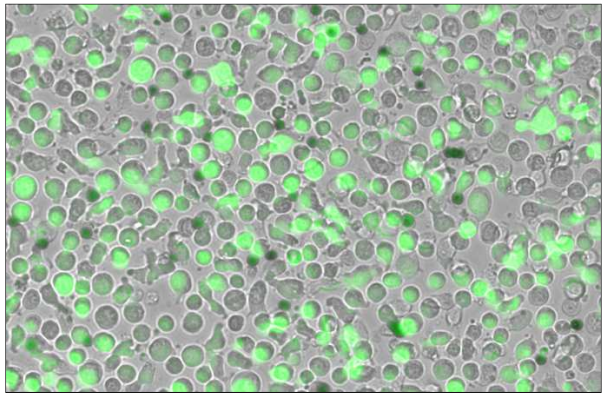
Fold expansion of Dynabeads® CD3/CD28 CTS™-activated T cells cultured in CTS™ OpTmizer™ T Cell SFM supplemented with CTS™ Immune Cell SR at 2%, 5%, 10%, or 2% Human AB serum (day 12).
N= 4 blood donors

CTS™ Immune Cell SR Supports Lentiviral Transduction of T cells Similar to Human Serum





T cells were transduced with a GFP-CAR lentiviral construct typically used in generating gene-modified T Cells (eg.g CAR19 and TCR

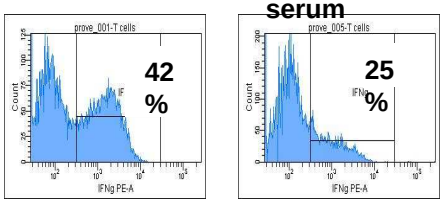


We thank James L. Riley and Andrew Medvec from the University of Pennsylvania, Department of Microbiology for providing the pELNS-GFP lentiviral vector

CTS™ Immune Cell SR Benefits

Intracellular IFNγ production

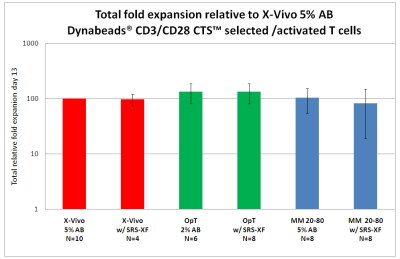
5% SRS-XF | **5% AB serum**



Superior Intracellular IFNγ production

CE-IVD
Meets USP 1043 Requirements for Ancillary Materials for Cell Gene and Tissue Engineered Products

Generic: Works with Standard Media



Security of Supply

Qualified suppliers
Multiple GMP sites

Traceable

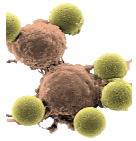
COO, COA, Donor Testing, DMF

Helps Save time

Minimize need to qualify serum

Immune Cell Qualified

Bead based QC Assay using primary T cells

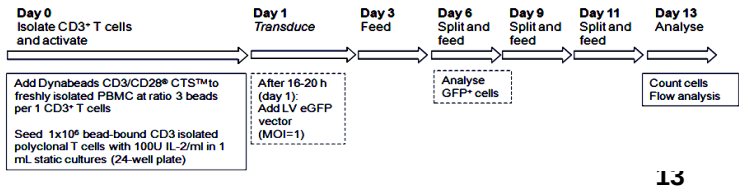


Scalable process

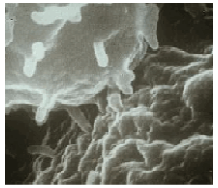
Flexible Use

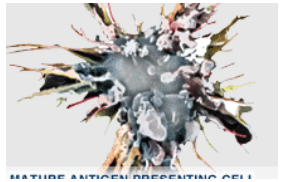
Regulatory compliant & commercial path

Superior performance

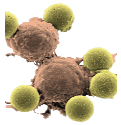


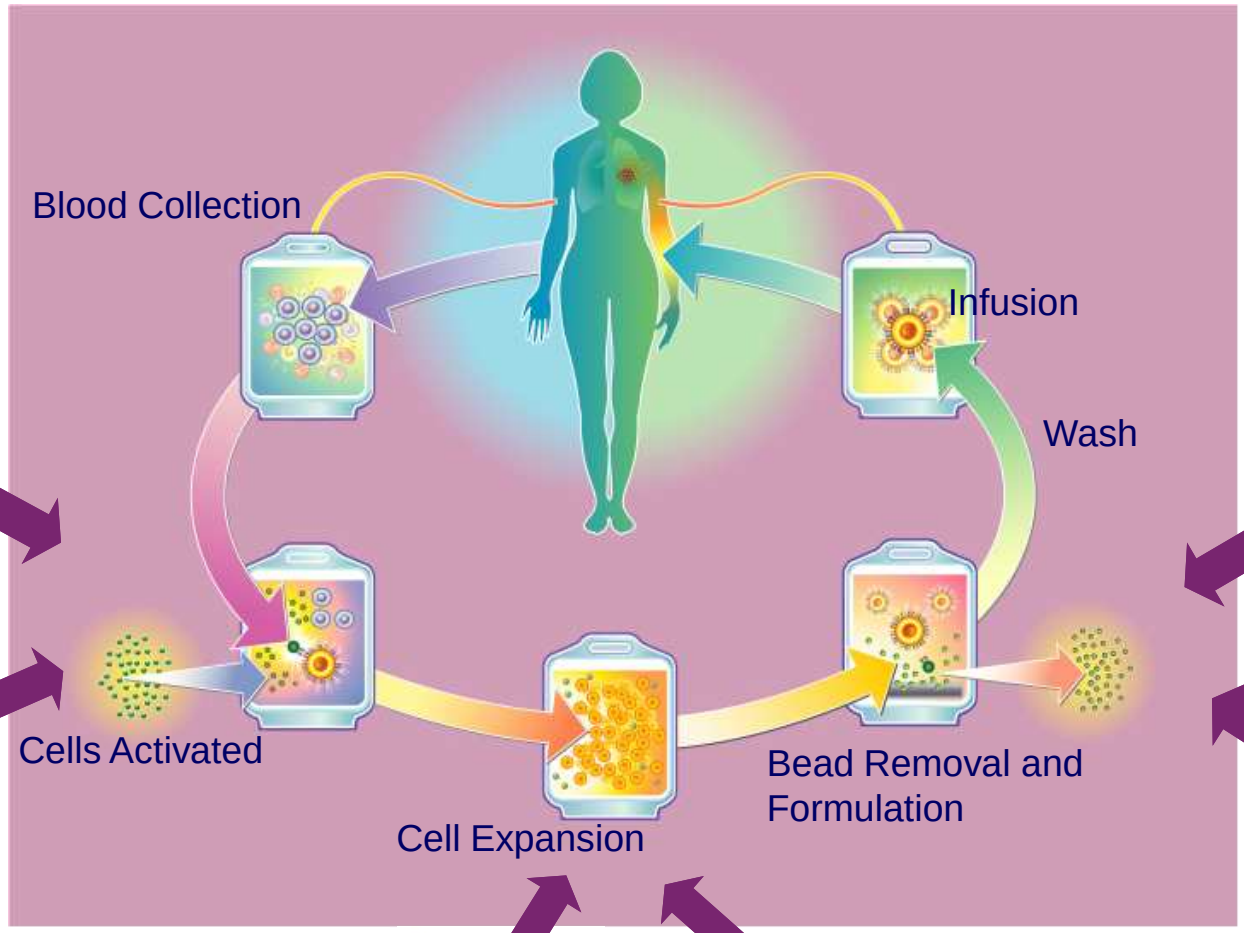
CTS™ Products Available for Your Immune Cell Workflow





CTS™ Dynabeads® CD3/CD28





CTS™DPBS

DynaMag™ CTS™ Magnet

CTS ™ AIM V
CTS™ OpTmizer™
CTS™ Immune Cell SR

CTS™ IL-2, IL-7
CTS™ GM-CSF, TNFα, IL-4

DynaMag™ CTS™ Magnet

Coming Soon!

CTS™ Immune Cell SR

Ordering Information:

A2596102 (500mL)

A2596101 (50mL)

Questions?

Please direct any questions to:
Sandy Kuligowski at sandra.kuligowski@lifetech.com

CTS™ Immune Cell SR is For In Vitro Diagnostic Use.

CTS™ Aim-V and CTS™ Optimizer are For human ex vivo tissue and cell culture processing applications. CAUTION: when used as a medical device, Federal Law restricts this device to sale by or non the order of a physician.

All other products are For Research Use or Manufacturing of Cell, Gene, or Tissue Based Products. CAUTION: Not intended for direct administration into humans and animals.