ONCOFIBRO™

TATMYCTOTRANS™

Myc Immune Modulator for Adoptive Cell Therapy

Tatmyctotrans™

Tatmyctotrans™ is a patented recombinant fusion protein comprising the MYC transcription factor fused to the TAT (Trans-Activator of Transcription) cell-penetrating domain, enabling efficient intracellular delivery. This transient, non-genetic approach enhances cell proliferation, survival, metabolism, and effector function while maintaining genomic integrity.

Tatmyctotrans™: A Breakthrough Ancillary Solution from Oncofibro

A next-generation ancillary reagent for adoptive cell therapy, designed to enhance immune cell performance throughout manufacturing and in vivo immune modulation

Challenges in Adoptive Cell Therapy

- Suboptimal starting material from stored research samples or heavily pretreated patients, often resulting in exhausted or anergic immune cells.
- Limited cell yield and expansion capacity, leading to insufficient numbers of functional therapeutic cells.
- Lengthy manufacturing timelines, typically requiring two to four weeks, which can delay treatment for rapidly progressing diseases.
- Manufacturing failures and product loss due to contamination, low gene transfer efficiency, or failure to meet release specifications.
- Logistical and shipping constraints that limit scalability and global accessibility

Tatmyctotrans™ delivers the 4E's of immune enhancement

- **Expanded Yield of Functional Therapeutic Cells** – MYC promotes proliferation, increasing viable high quality T cells ready for infusion.
- **Enhanced Metabolic Fitness** – Activates glycolysis, glutaminolysis, and oxidative phosphorylation for energy and biosynthesis.
- **Efficient Gene Transfer** – MYC shifts cells into favorable cycling phases, improving viral and non-viral transduction efficiency.
- **Effective Functional Restoration** – Restores effector cytokine production, cytotoxic activity, and overall immune responsiveness in exhausted or anergic cells

Integration into Cell Therapy Manufacturing Workflows

Tatmyctotrans™ is designed to be seamlessly integrated at multiple stages of the adoptive cell therapy (ACT) workflow, offering a versatile alternative to IL-2 with comparable benefits but minimal to no systemic toxicity. It can be applied during various stages of manufacturing:

1 Activation / Priming (Day 0–2)

Current hurdles:

T cells from cancer or chronic viral infection patients often show anergy or exhaustion after chronic antigen exposure, responding poorly to CD3/CD28 stimulation.

Tatmyctotrans™ Advantages:

a. Reverses anergy/exhaustion by restoring MYC-driven transcription, metabolic activity, and effector programs.

b. Expands the pool of metabolically fit, responsive T cells ready for engineering.

c. Also shifts more cells into active cycling phases (G1/S/G2), preparing them for efficient gene transfer later.

2 Genetic Transduction (Day 2–3)

Current hurdles:

Viral vectors (lentiviral/retroviral) are introduced into activated T cells, but uptake can be limited in poorly cycling or metabolically weak cells.

Tatmyctotrans™ Advantages:

a. Maintains high metabolic activity and cycling rates from Step 1.

b. Increases viral gene transfer efficiency and transgene expression.

c. Can shorten the post-transduction expansion time.

3 Expansion with Cytokines (Day 3–11)

Current hurdles:

Cells are expanded with IL-2, IL-7, or IL-15; exhausted cells expand poorly and require high cytokine doses.

Tatmyctotrans™ Advantages:

a. MYC-driven metabolic reprogramming boosts nutrient uptake and biosynthesis.

b. Sustains proliferation and viability without excessive cytokine support.

c. Maintains a balanced memory/effector phenotype for long-term in vivo persistence.

4 Final Formulation & Cryopreservation

Current hurdles:

CAR-T products lose some viability and function after cryopreservation.

Tatmyctotrans™ Advantages:

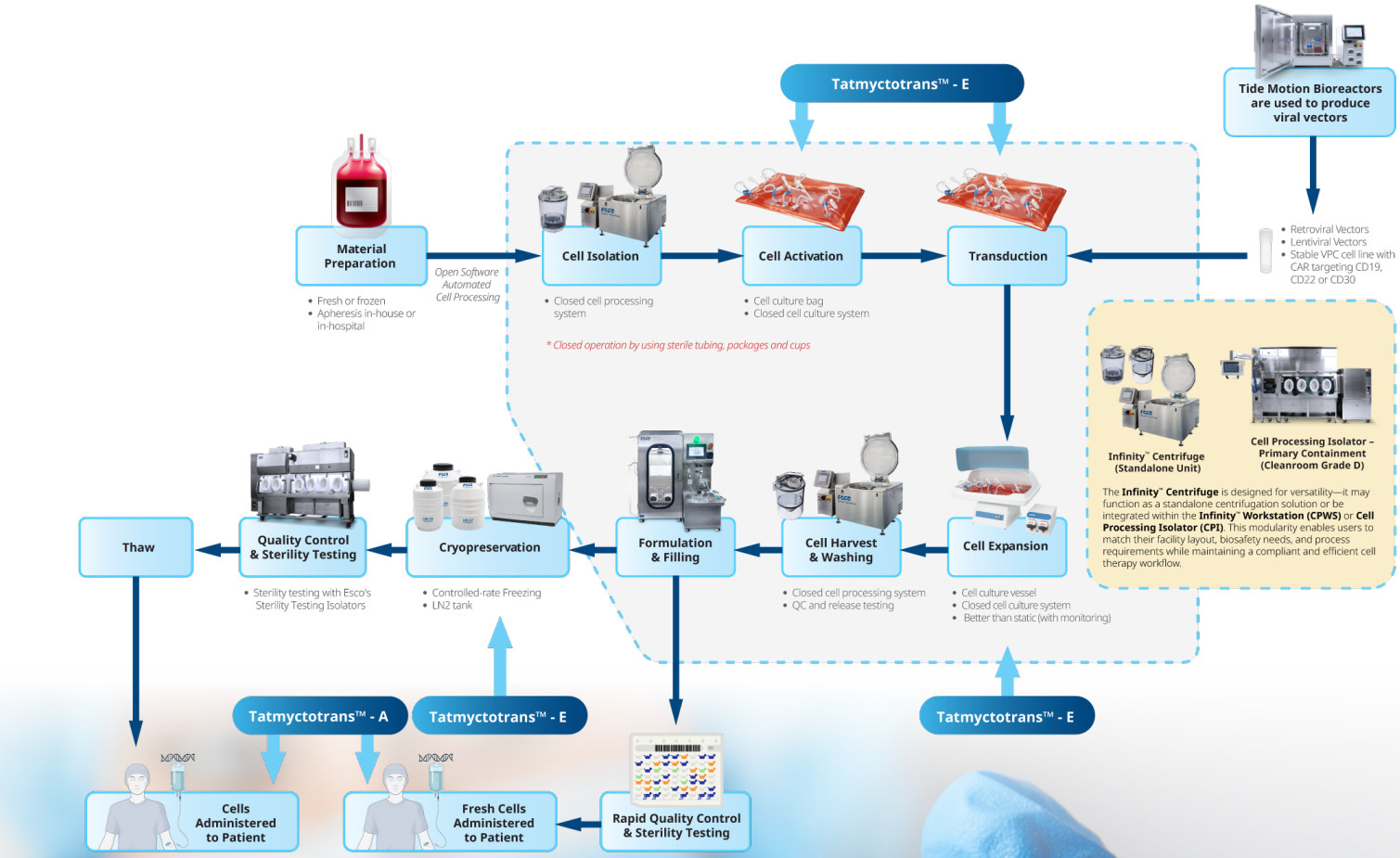
a. Increases total yield of functional T cells at harvest.

b. Improves post-thaw recovery, viability, and functional potency.

Tatmyctotrans™: A Dual-Mode Platform

- **Ex Vivo Enhancer (Research Use and Clinical-Grade)**
  Tatmyctotrans™-E enhances ex vivo manufacturing of chimeric antigen receptor T cells, T cell receptor–engineered T cells, tumor-infiltrating lymphocytes, natural killer cells, gamma delta T cells, and dendritic cell therapies. It supports research use, good laboratory practice toxicology, and pharmacokinetic and pharmacodynamic studies, enabling transition from preclinical to clinical development. The protein is transiently active and naturally degraded within approximately five days.

- **In Vivo Immunomodulator (Current Good Manufacturing Practice Grade)**
  Tatmyctotrans™-A is intended for in vivo use as an adjuvant, neoadjuvant, or standalone immunomodulatory therapy for cancer. Its short biological persistence, with degradation within approximately five days, enables transient immune modulation with a favorable safety profile.



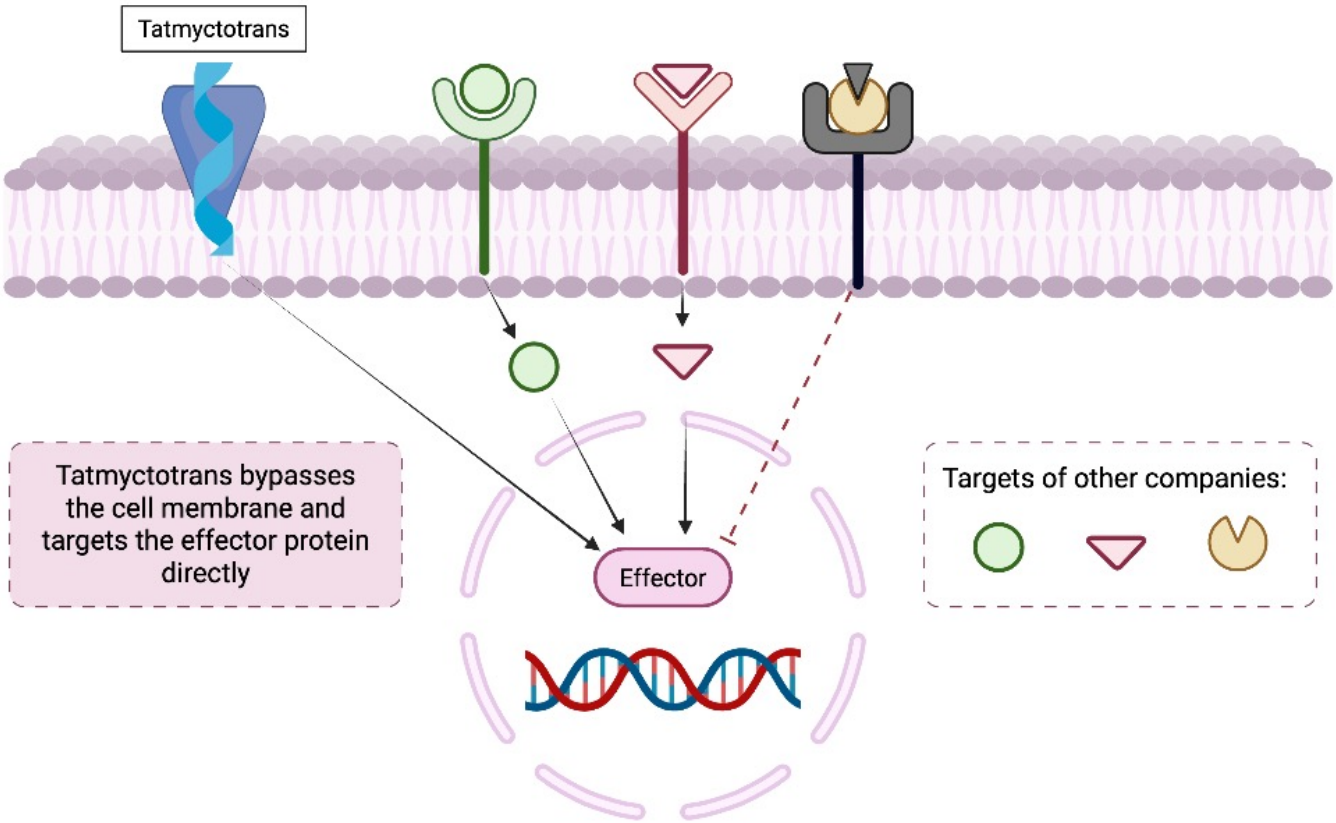
Tatmyctotrans™: Mechanism of Action

TAT

- The TAT protein transduction domain is derived from the Trans-Activator of Transcription, a protein originally encoded by human immunodeficiency virus type 1. It contains a short, positively charged amino acid sequence that enables direct, receptor-independent penetration of cell membranes.
- This natural cell-penetrating property has been repurposed as a delivery module to efficiently transport therapeutic cargos, such as proteins, peptides, or nucleic acids, into mammalian cells in a manner compatible with good manufacturing practice workflows.
- TAT offers: Receptor-independent, Gentle and transient, an Efficient and scalable

MYC

- MYC is a transcription factor that serves as a central regulator of cell growth, metabolism, and proliferation. It controls the expression of genes involved in ribosome biogenesis, energy production, cell-cycle progression, and multiple biosynthetic pathways that support cellular expansion and function.
- In immune cells, tightly regulated MYC activity is essential for activation, clonal expansion, metabolic fitness, and effector function. Importantly, transient modulation of MYC activity can enhance immune cell performance while avoiding permanent genetic alteration, enabling a controllable and reversible approach to immune cell modulation.



The Tat protein transduction domain is the most extensively validated cell-penetrating peptide and efficiently delivers large fusion proteins, making it ideal for platforms such as Tatmyctotrans™. Tatmyctotrans™ bypasses membrane signaling and delivers MYC directly into cells, where MYC's intrinsic nuclear localization signals drive nuclear accumulation and transcriptional reprogramming. This **non-genetic, transient protein delivery** enhances metabolic fitness, proliferation, and functional recovery of exhausted or anergic lymphocytes.

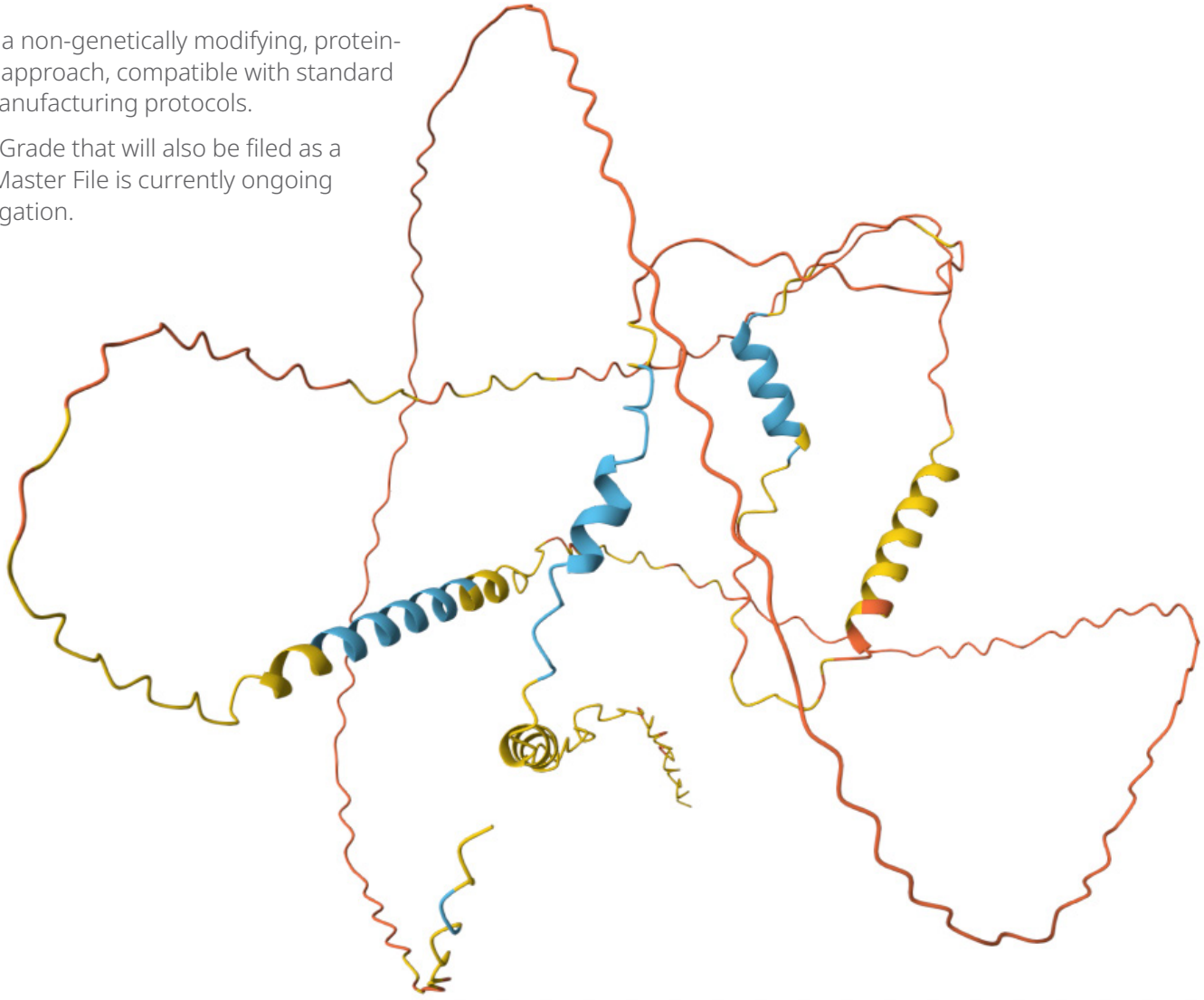
Regulatory & Manufacturing Readiness

Tatmyctotrans™ is currently available in RUO, Clinical, and GMP grades (ISO 13485 / USP 1043) and:

- Is supported by a US FDA Type II Master File
- Is cited in active INDs and filings in the US, EU, Japan, and Israel
- Is currently used in multiple clinical trials for oncology and infectious disease
- Is designed for ex vivo use only — for further manufacturing and/or cryopreservation

This is a non-genetically modifying, protein-based approach, compatible with standard ACT manufacturing protocols.

cGMP Grade that will also be filed as a Drug Master File is currently ongoing investigation.



Summary — Why Tatmyctotrans™

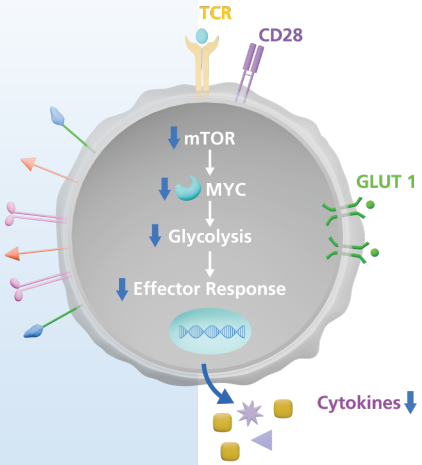
- Boosts proliferation and expansion of exhausted and low-yield T cell populations
- Enhances gene transduction and metabolic activity without receptor dependency
- Reduces immune checkpoint markers, improving effector function
- Integrates into a wide range of ACT modalities
- Backed by global regulatory filings and ongoing clinical use

How Tatmyctofusp Works: Reactivating T Cells from Exhaustion

T CELL EXHAUSTION

Persistent Antigen Exposure Suppresses T-Cell Metabolism

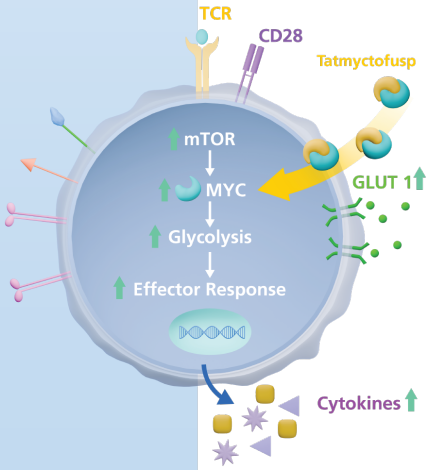
Chronic antigen stimulation causes T-cell exhaustion marked by increased PD-1/TIM-3/TIGIT expression. This checkpoint signalling suppresses AKT–mTOR–MYC pathways, reducing glycolysis and effector function.



REPLENISHMENT OF MYC

Tatmyctofusp Delivery & Bypass of Checkpoint Blockade

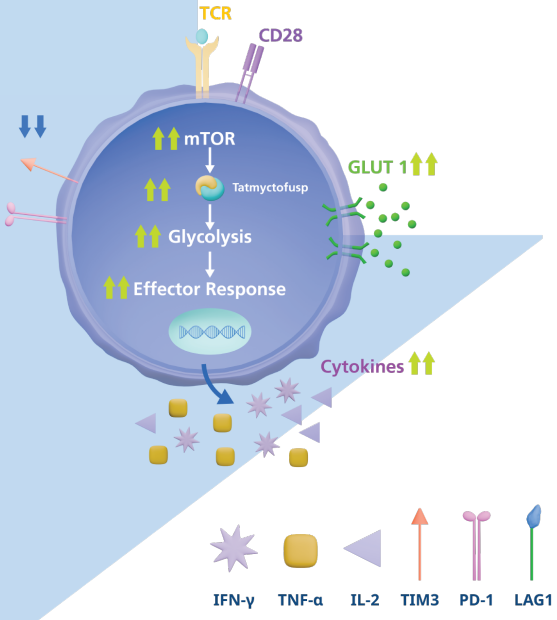
Tatmyctofusp penetrates the T cell and restores MYC-dependent transcriptional programs, reactivating glycolysis and biosynthetic pathways despite ongoing checkpoint inhibition.



REVERSAL OF EXHAUSTION

Metabolic Re-Engagement Reverses Exhaustion and Restores Function

Restored metabolic fitness drives a shift away from the exhausted phenotype, reducing inhibitory receptor expression and enhancing effector function and proliferation



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