Updates on mRNA Therapeutic Vaccine Programs

March 2025

Agenda

01 Everest Medicines mRNA Platform and Pipeline Introduction

02 mRNA Personalized Cancer Vaccine Program (PCV)

03 mRNA Tumor associated antigen (TAA) Cancer Vaccine Program

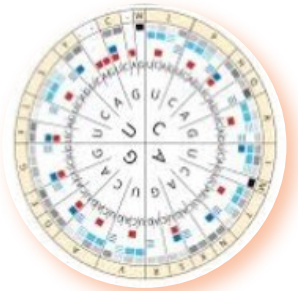
04 mRNA in-vivo CAR-T Program

EVEREST MEDICINES

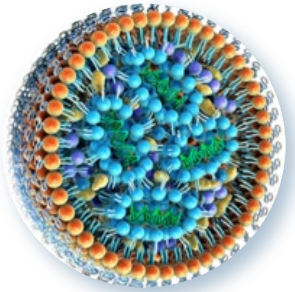
Everest Medicines mRNA Platform and Pipeline Introduction

EVEREST MEDICINES

A Fully Integrated and Clinically Validated mRNA Platform



Proprietary antigen design algorithm ensures high expression of target antigen



Proprietary LNP delivery system leads to enhanced T cell immunity

CMC process development ensures robust mRNA DS/DP production

Self-owned manufacturing facility (Jiashan, Zhejiang) successfully produced GMP material

End-to-end capabilities across the whole value chain of mRNA platform

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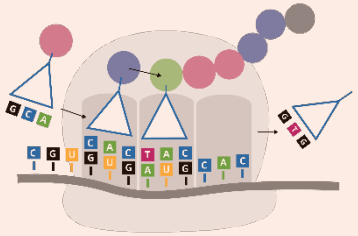
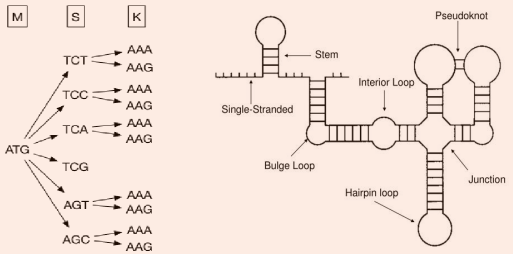
Proprietary mRNA Sequence Design Algorithm Enabled by AI Modeling

Optimize codon usage and minimize sequence liabilities



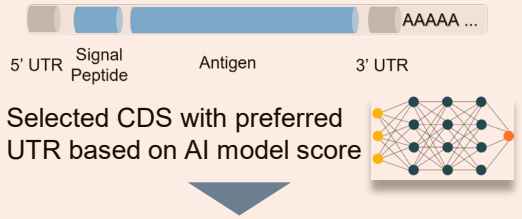
1st Gen

Co-optimize codon and RNA secondary structure



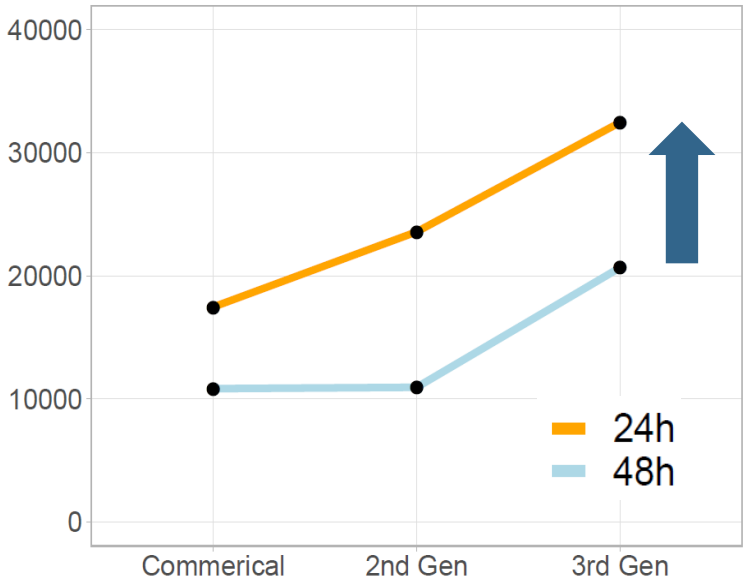
2nd Gen

AI scoring model to co-optimize UTR and CDS

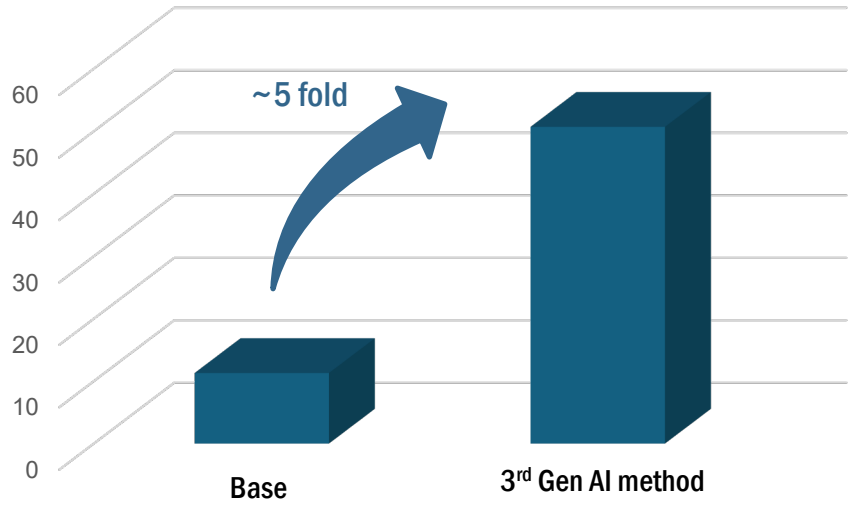


3rd Gen

eGFP mRNA Optimization



Target Protein Expression



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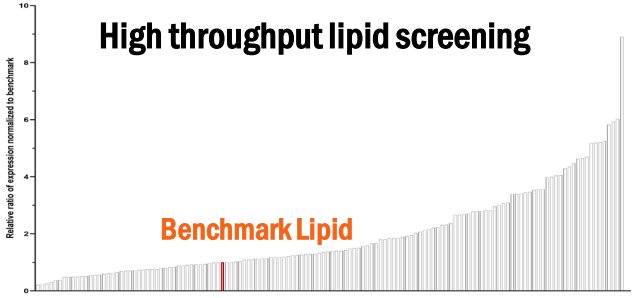
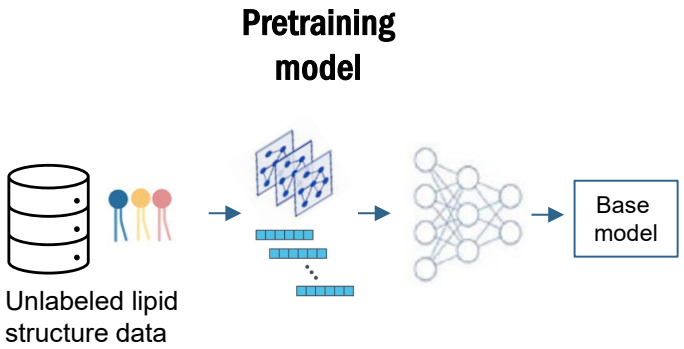
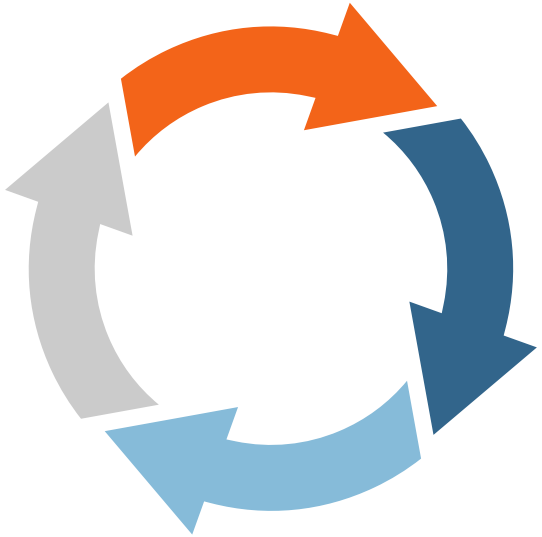
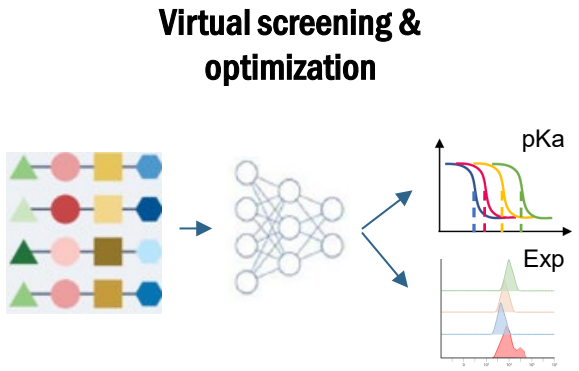
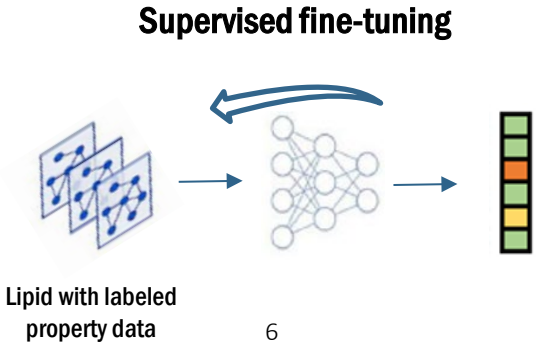
Proprietary LNP Delivery System with Novel Ionizable Lipid











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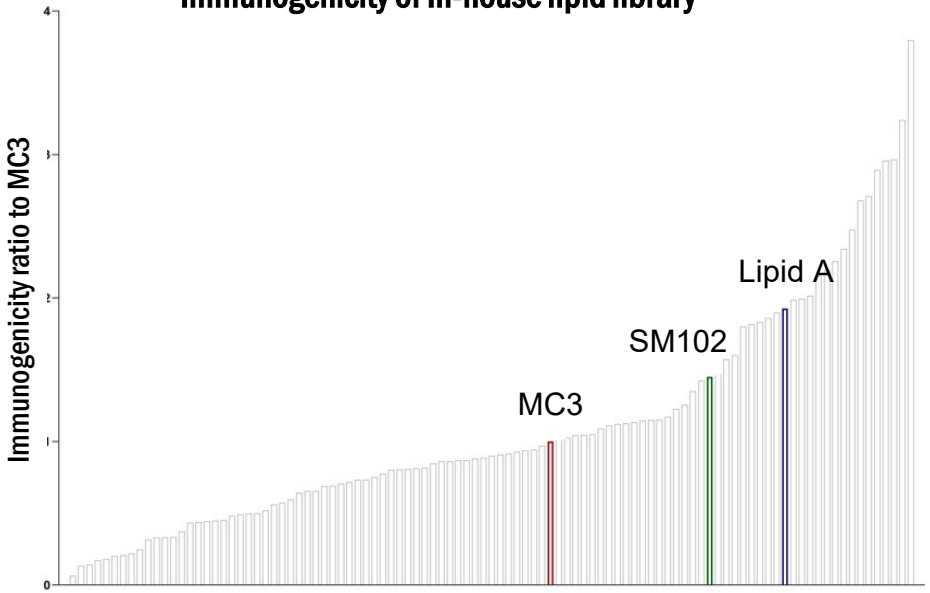
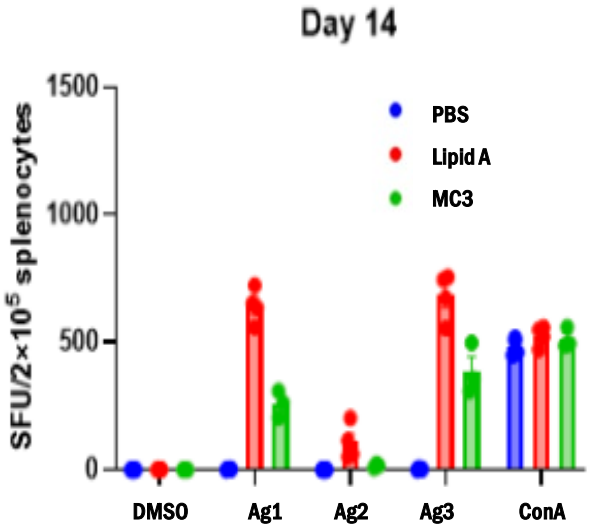
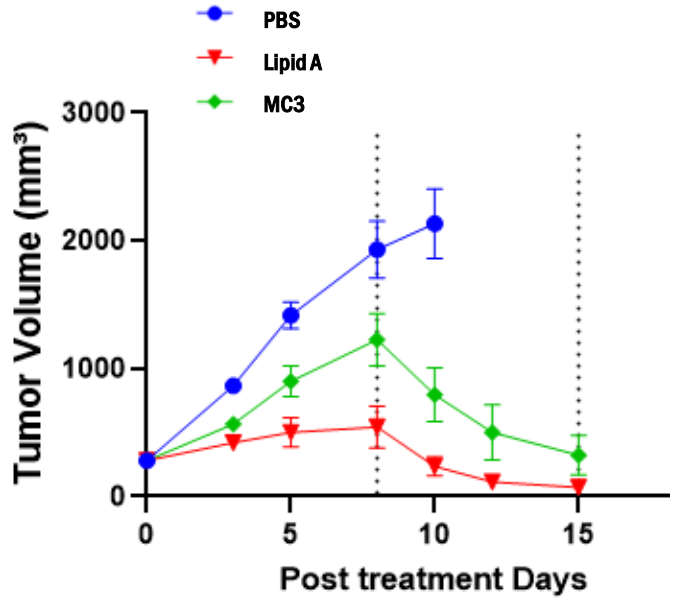
Proprietary Ionizable Lipid Candidates for Cancer Vaccine

Immunogenicity of In-house lipid library

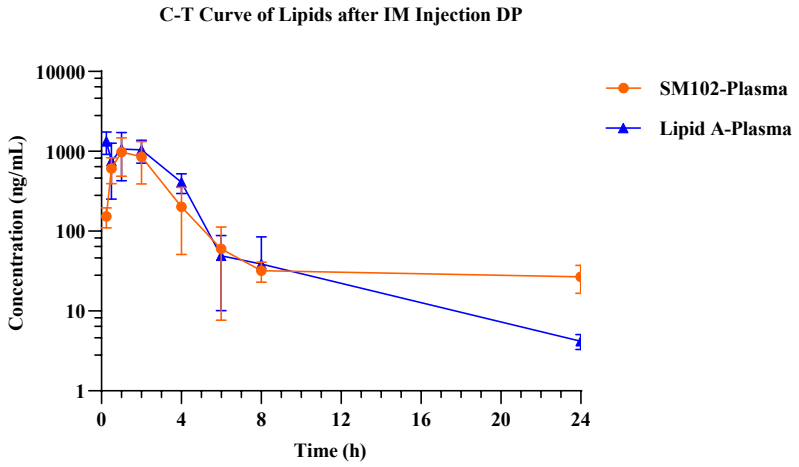


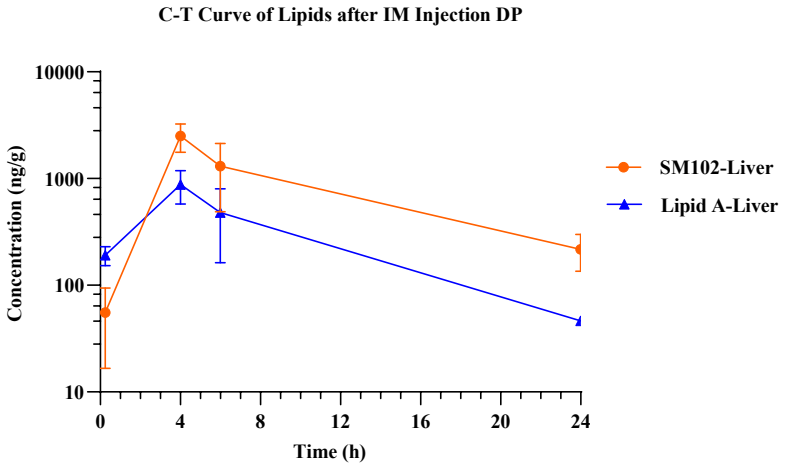
Higher immunogenicity is associated with better efficacy in mouse tumor model





SD Rat PK results showed a fast clearance in plasma and liver





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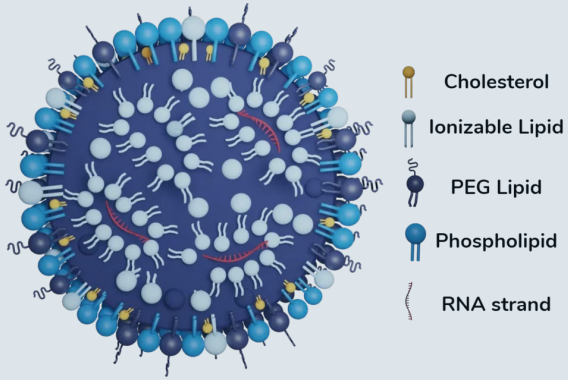
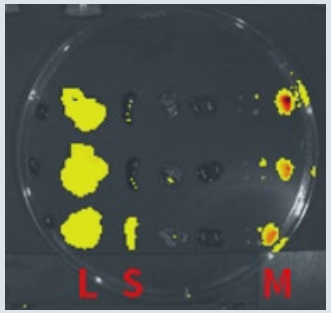
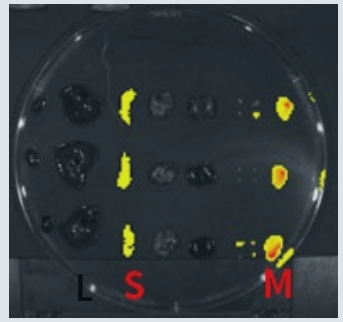
Proprietary Delivery System Can Achieve Tissue/Cell Specific Delivery via Passive and/or Active Targeting



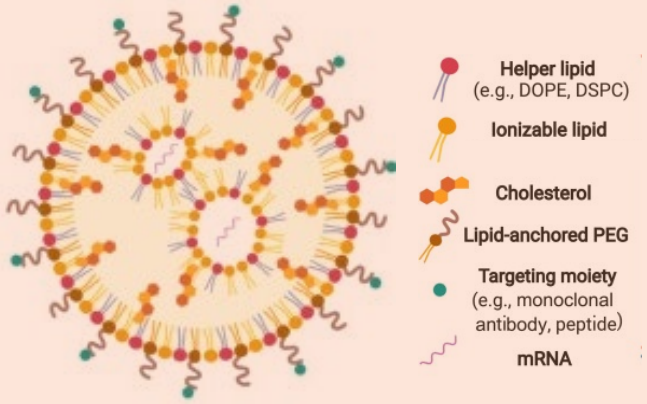
Classic LNP

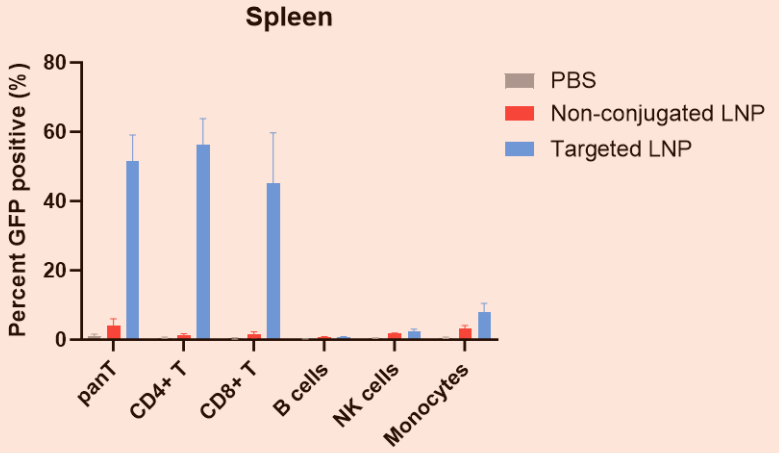


Proprietary LNP



L-liver; S-spleen; M-Injection site





EVEREST MEDICINES

A Growing Pipeline of mRNA-Based Therapeutics

- Personalized cancer vaccine (PCV) EVM16 has commenced an investigator-initiated trial in China. **FPD achieved on March 4.**
- Off the shelf TAA cancer vaccine EVM14 has completed IND-enabling studies and **submitted IND in US in February.**
- In vivo CAR-T program has completed a **NHP study** and continues to progress towards preclinical candidate selection.

	mRNA platform			
	Personalized Cancer vaccines	TAA cancer vaccines	Immune-modulatory cancer vaccines	In vivo CAR-T
Indication	Cancer	Cancer	Cancer	Cancer /Autoimmune
Development Status	Launched IIT	US IND submitted in Feb 2025	IND filing in 2025-2026	Pre-clinical POC 4Q 2024

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mRNA Personalized Cancer Vaccine Program (PCV)

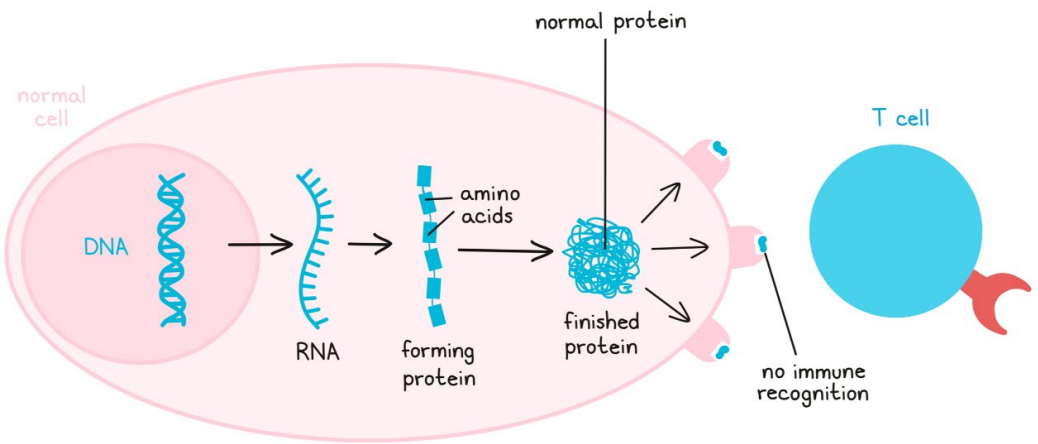
EVEREST MEDICINES

Neoantigens are Widely Used in Cancer Vaccines

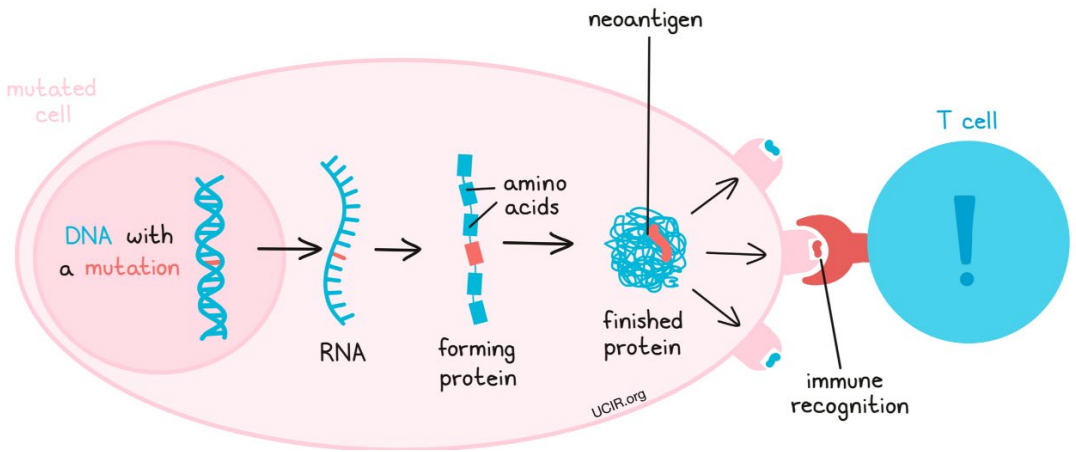
Neoantigens:

- A new protein that only forms on cancer cells when certain mutations occur in tumor DNA.
- Neoantigens may play an important role in helping the body make an immune response against cancer cells.
- Neoantigens used in vaccines and other types of immunotherapy are being studied in the treatment of many types of cancer.

Normal cells



Tumor cells with somatic mutations



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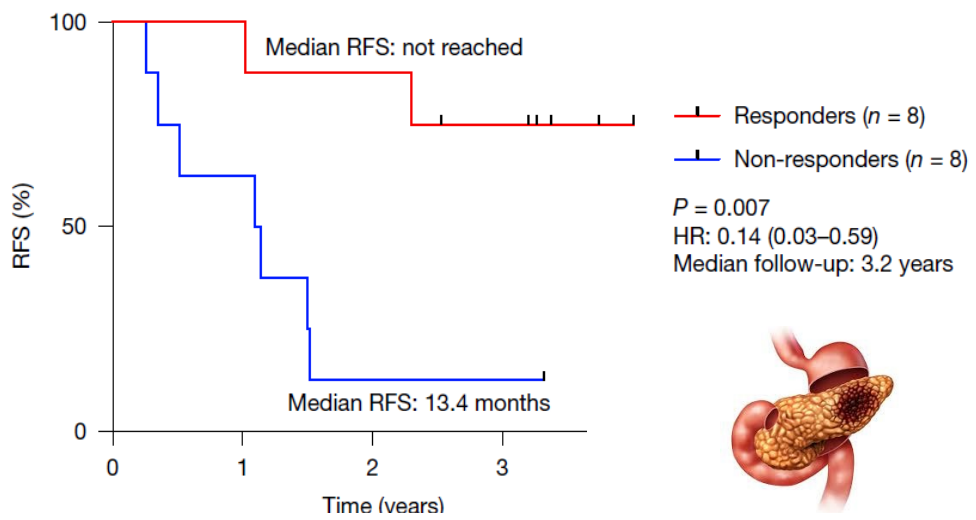
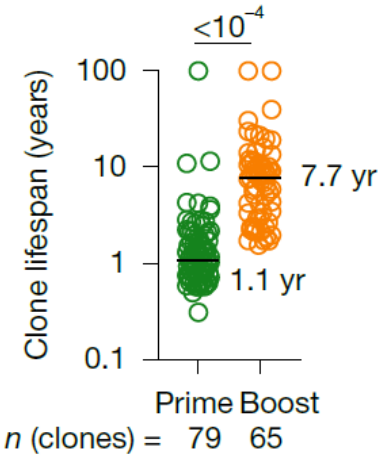
Personalized Cancer Vaccines Significantly Reduces Recurrence Risk and Enhances IO Response in Multiple Cancer Types

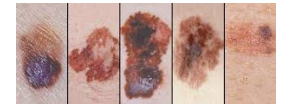
BIONTECH — Autogene cevumeran

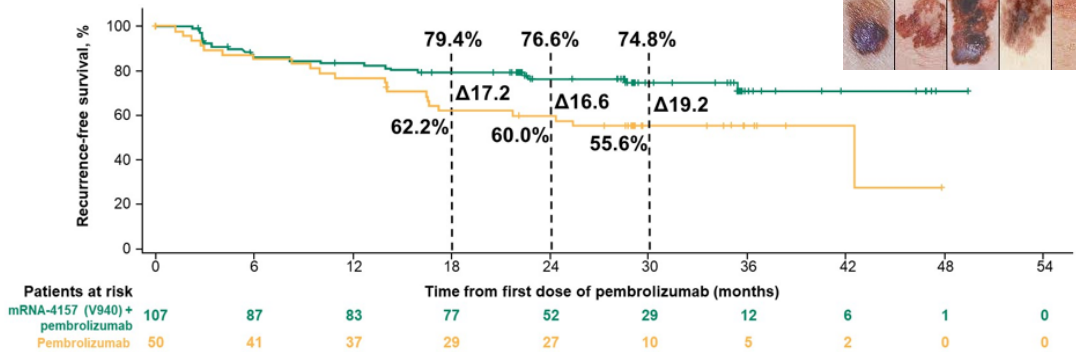




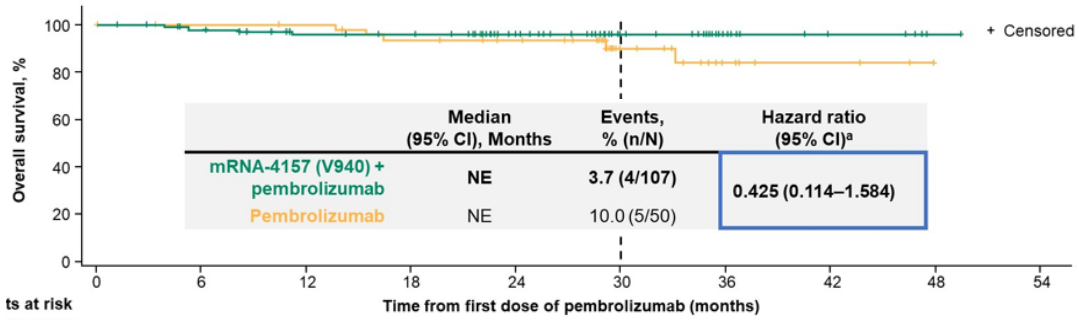
- At 3.2 years follow-up, 75% responders were recurrence-free; recurrence risk of responders was reduced by 86% compared with non-responders
- After booster administration, neoantigen-specific CD8+ T cell clones have an average estimated lifespan of 7.7 years，~20% of clones have multi-decade lifespans

moderna — mRNA-4157





	Median (95% CI), months	Events, % (n/N)	Hazard ratio (95% CI)[a]
mRNA-4157 (V940) + pembrolizumab	NE	23.4 (25/107)	0.510 (0.288–0.906) P = 0.019[b]
pembrolizumab	42.51 (16.59–NE)	44.0 (22/50)	



	Median (95% CI), Months	Events, % (n/N)	Hazard ratio (95% CI)[a]
mRNA-4157 (V940) + pembrolizumab	NE	3.7 (4/107)	0.425 (0.114–1.584)
Pembrolizumab	NE	10.0 (5/50)	

- At 3 years follow-up, recurrence risk was reduced by 49% compared with pembrolizumab alone; death risk showed an encouraging reducing trend

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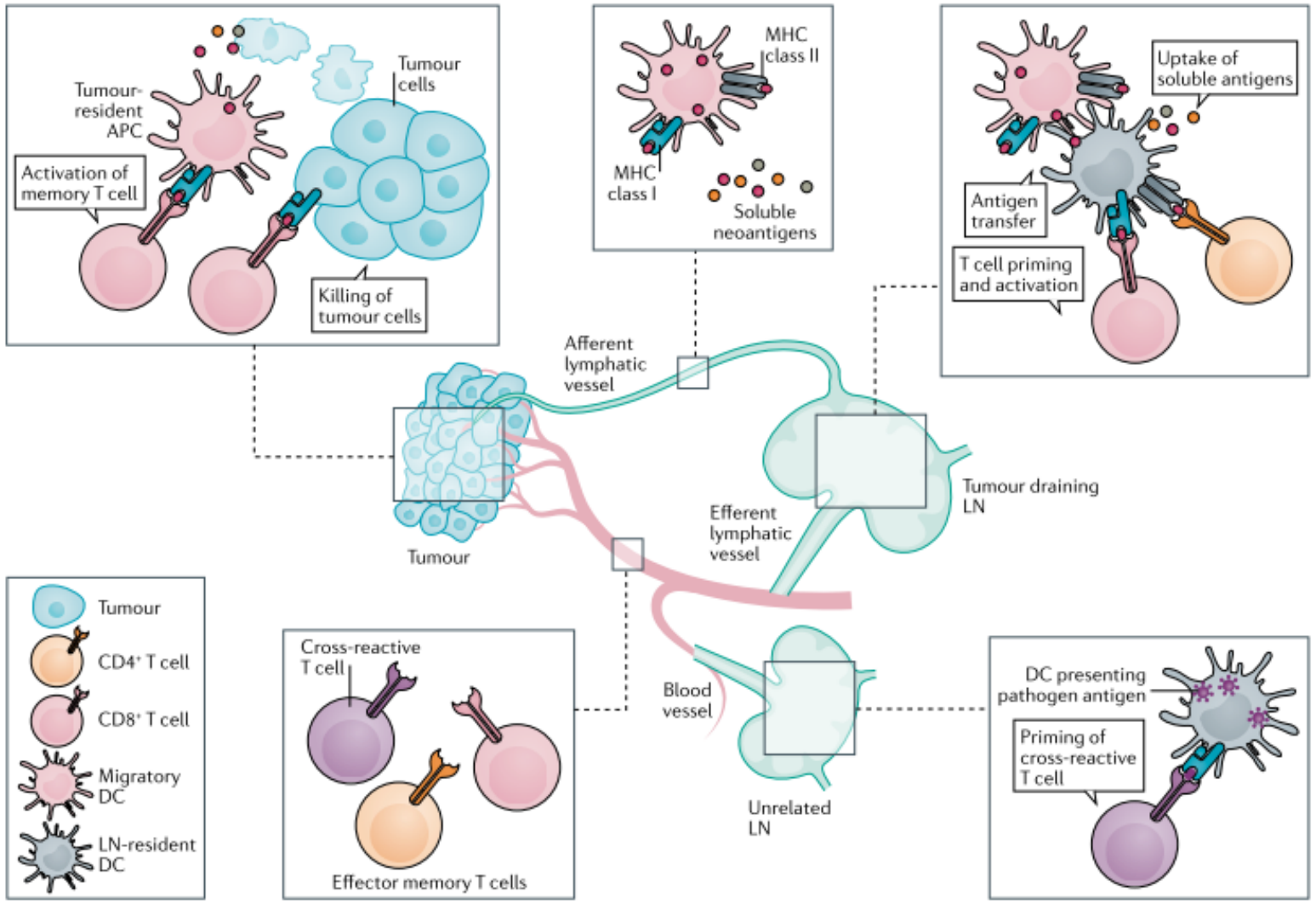
Neoantigens can Induce T Cell Response and Tumor Cell Killing



Requirement for inducing robust neoantigen T cell response and tumor killing

- Somatic mutations
- Mutation is expressed
- Presentation
- Availability of neoantigen specific or cross-reactive T cells
- Priming (by vaccination)
- High mutation clonality

Lang et al. (2022) Nature Reviews Drug Discovery

EVEREST MEDICINES

Everest Medicine's Proprietary Machine Learning Based Neoantigen Prediction Algorithm (EVER-NEO-1)

Tumor sample

PBMC sample

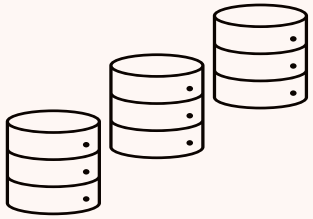
Exom-seq & RNA-seq

Mutation, HLA calling & expression analysis

Somatic mutation & expression filtering

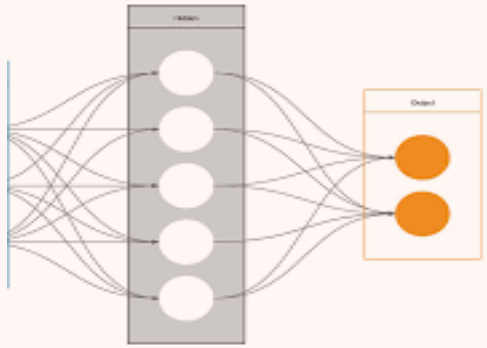
Candidate neoantigen sequence

Machine Learning (ML) based prediction algorithm



Human & mouse immunogenicity datasets

- MHC binding strength/number
- Differential binding
- Pathogen seq similarity
- WT/MT seq change distance
- ...



MHC I and II epitope scoring DN Models

Top 20 peptide immunogenicity % in independent testing data

	MHC I	MHC II
Human	60%	85%
Mouse	90%	50%

Epitope/peptide Immunogenicity score

Top peptides for mRNA design

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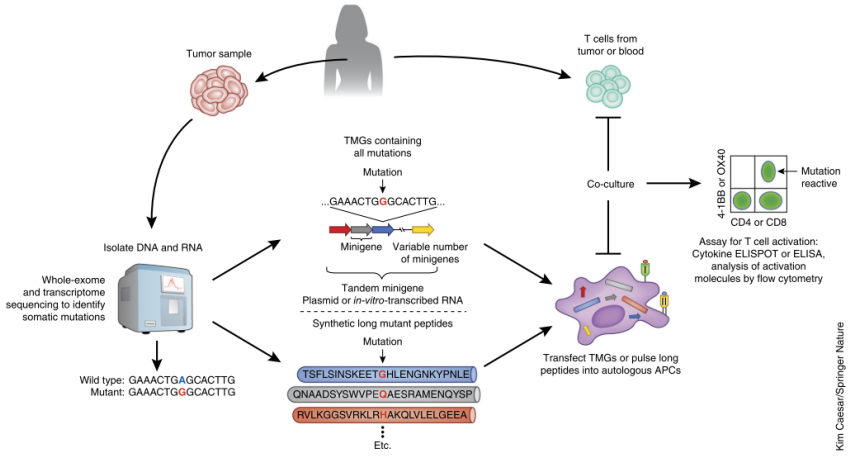
EVER-NEO-1 Method Validated On Human Neoantigen Immunogenicity Data

Neoantigen-reactive TIL screening data in cancer patients



57 TIL reactive MHC I neoantigens in 7180 mutations from 39 patients (CRC, STAD, CHOL and PAAD)

Test the ability to capture immunogenic mutations in each patients

Pos #	EVER-NEO-1	MSKCC
Top 20	29/39 (74.4%)	20/39 (51.3%)
Top 30	33/39 (84.6%)	25/39 (64.1%)
Top 34	34/39 (87.2%)	26/39 (66.7%)

Published PCV mRNA vaccine phase 1 study immunogenicity data

T cell Response	Total Neoantigens		CD8 Neoantigens		CD4 Neoantigens	
	Number	Detection Rate	Number	Detection Rate	Number	Detection Rate
Med	78	75.6%	69	75.4%	15	80%
High	29	79.3%	25	84%	9	77.8%

EVEREST MEDICINES

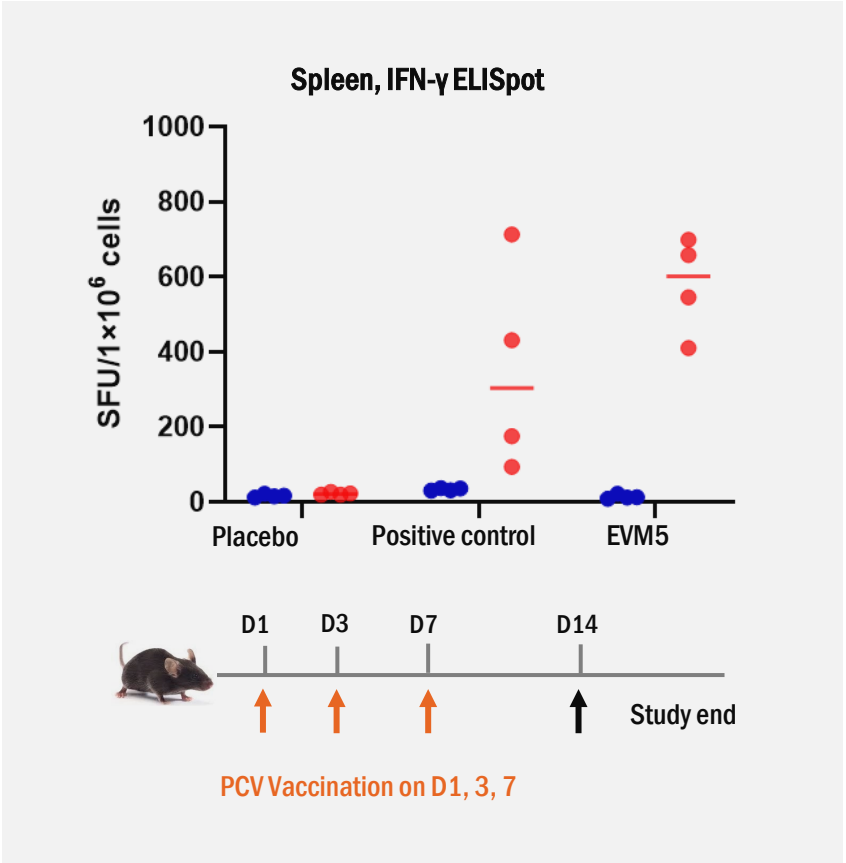
PCV Vaccine Designed with EVER-NEO-1 Demonstrates Superior Immunogenicity and Efficacy

WES,
RNAseq

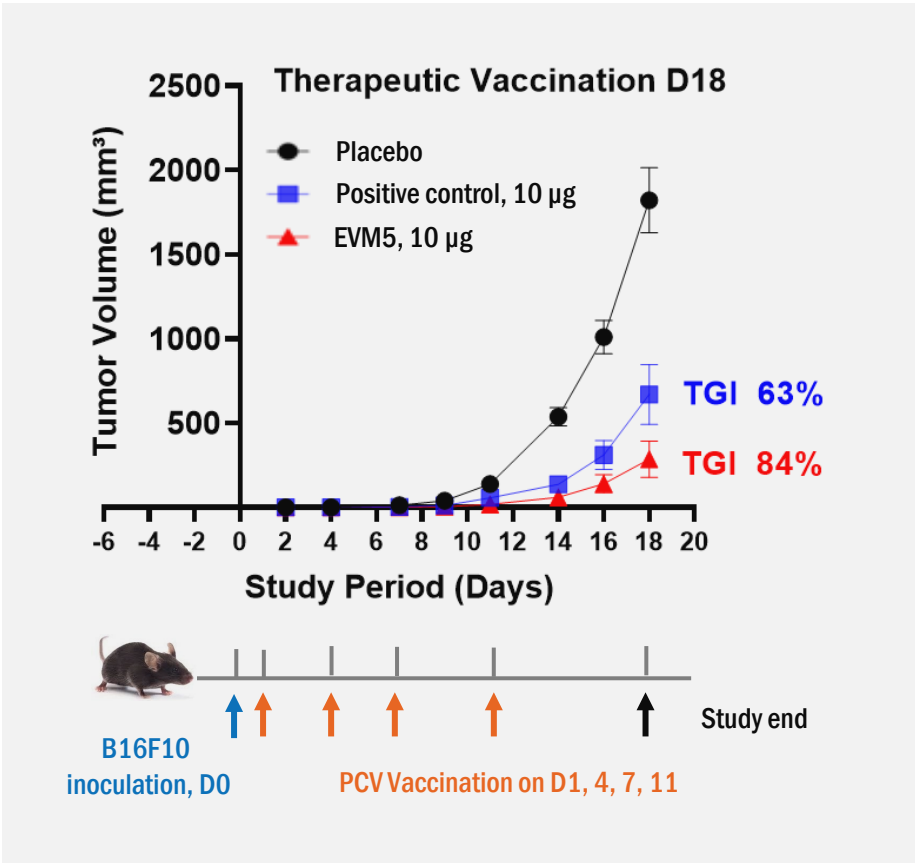
EVER-NEO-1

EVM5

High Immunogenicity in naive mice



Superior efficacy in syngeneic tumor model



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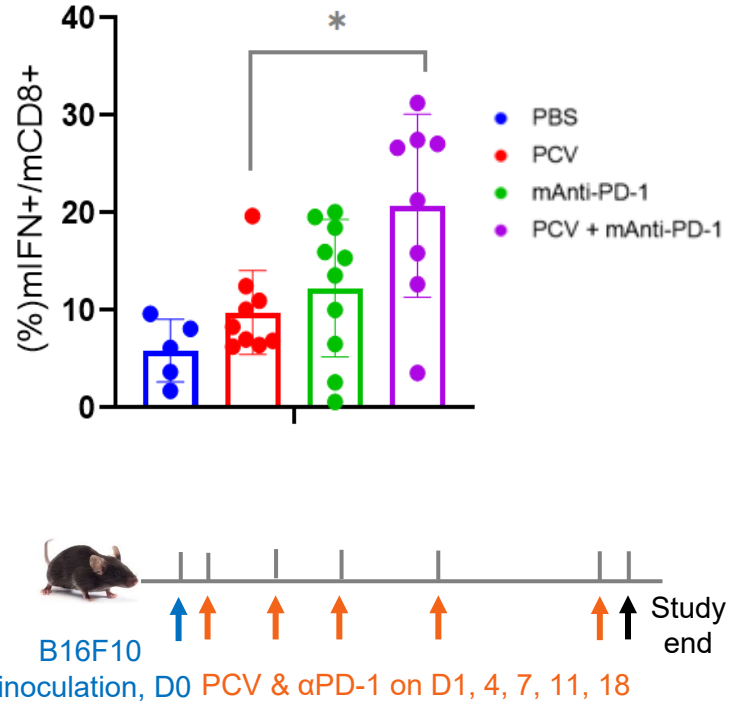
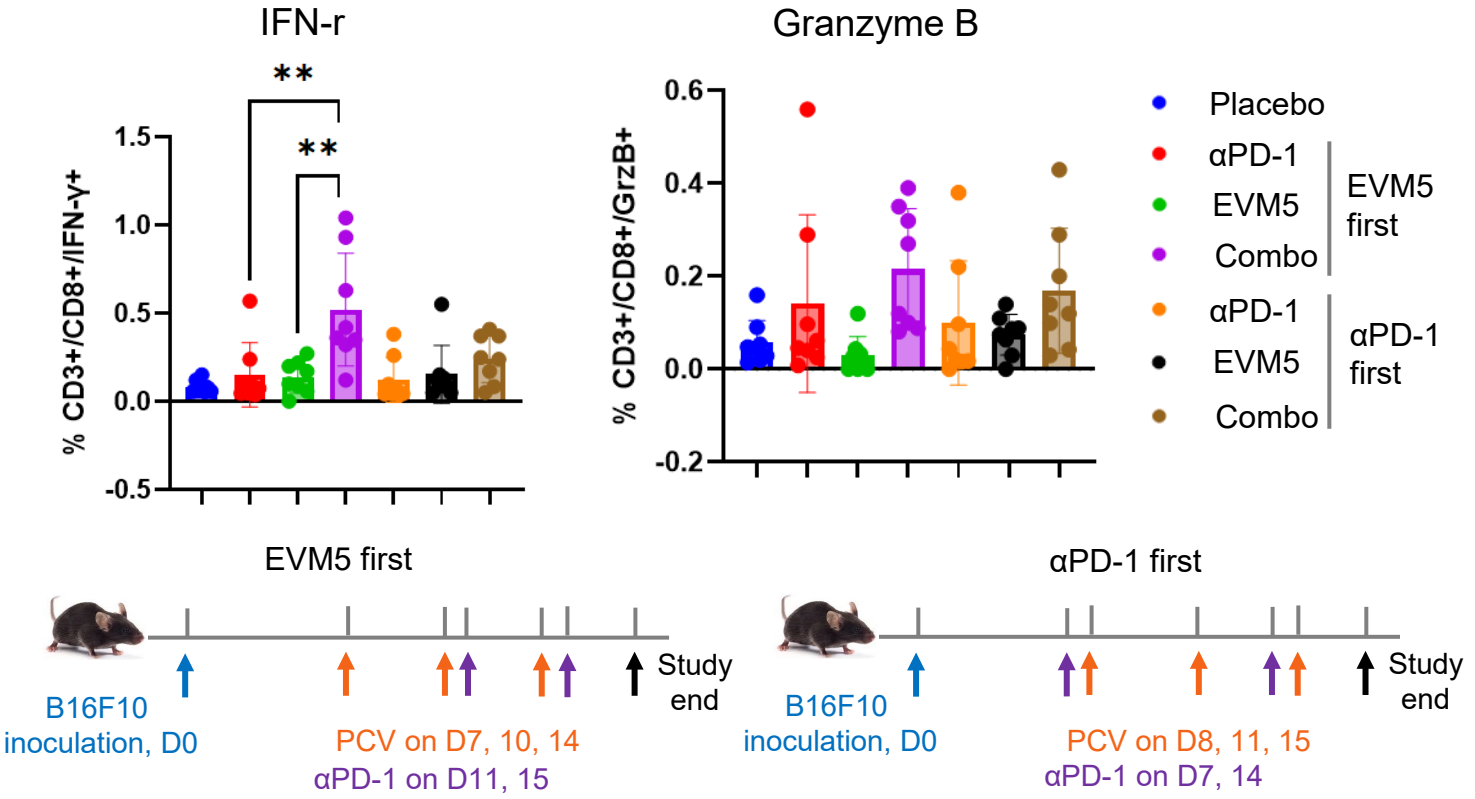
PCV Vaccine Combo with αPD-1 Showed Synergistic Effect in T cell Activation

Early treatment setting



Advanced disease setting



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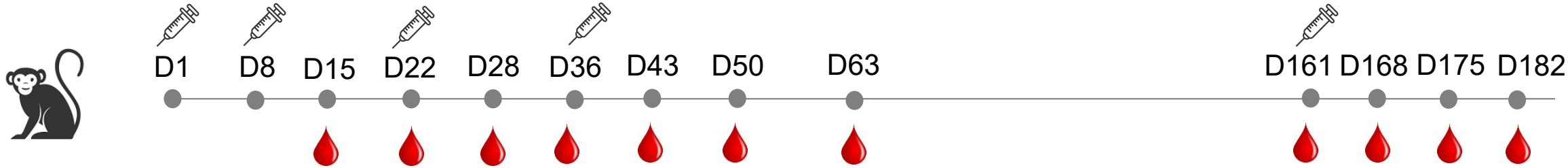
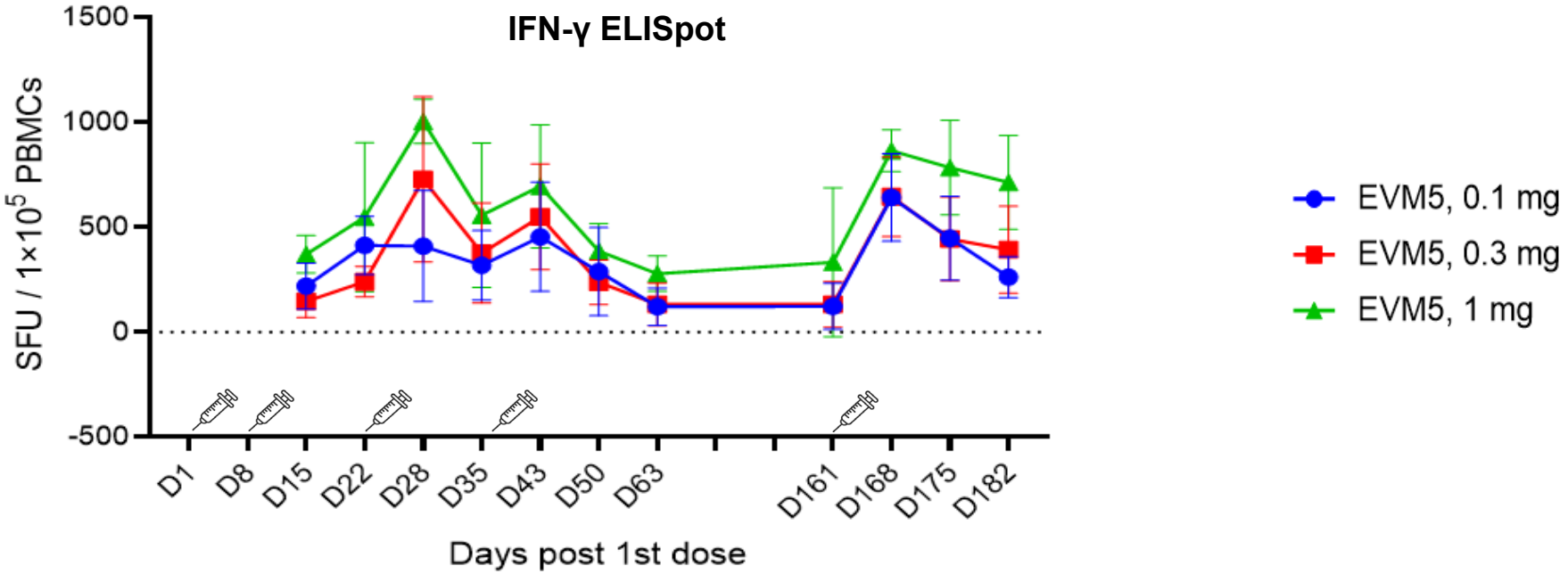
PCV Stimulates Potent and Sustainable T cell Response in Rhesus Monkey



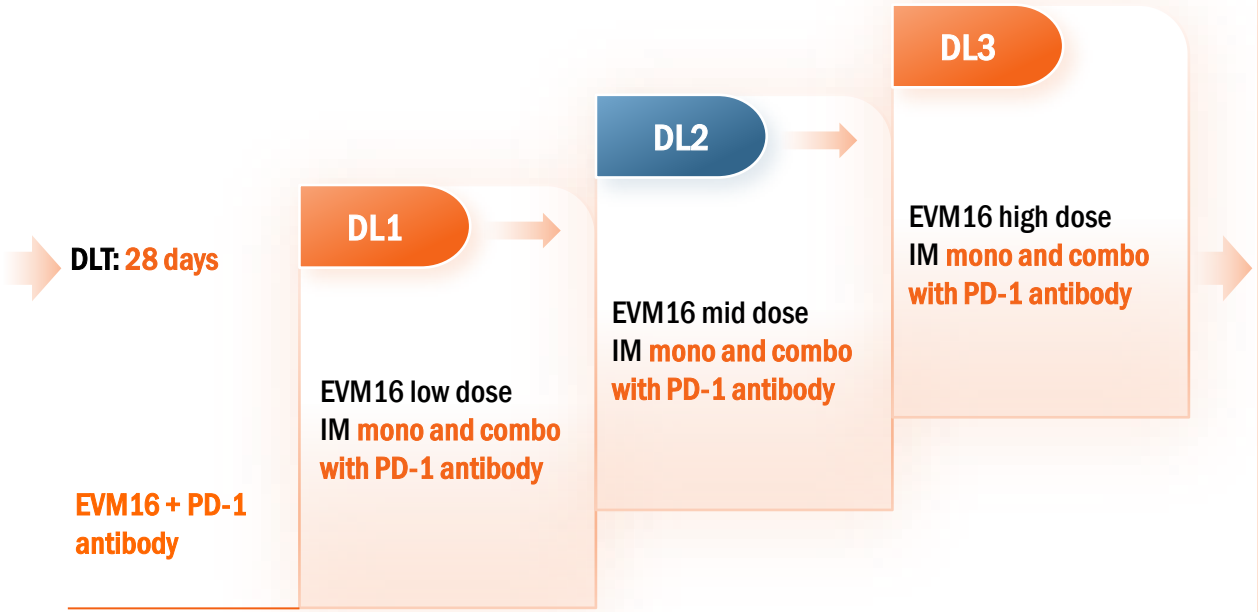


EVM5, the preclinical surrogate of EVM16, stimulate potent and persistent T cell response in monkey

EVEREST MEDICINES

EVM16 IIT Study Launched in Two Top Cancer Hospitals In China (NCT06541639)

- Recurrent or metastatic solid tumors that have been histologically or cytologically pathologically confirmed and are not amenable to radical treatment with surgery or local therapy.
- Patients with advanced or recurrent solid tumors who have failed prior standard therapy.



Primary endpoints:

- safety, tolerability, determine RP2D of EVM16

Secondary endpoints:

- Immunogenicity (neoantigen specific T cell responses)
- ORR, DoR, DCR, TTR, PFS

复旦大学附属肿瘤医院 Fudan University Shanghai Cancer Center

北京大学肿瘤医院 BEIJING CANCER HOSPITAL

FPD Achieved on March 4, 2025

EVEREST MEDICINES

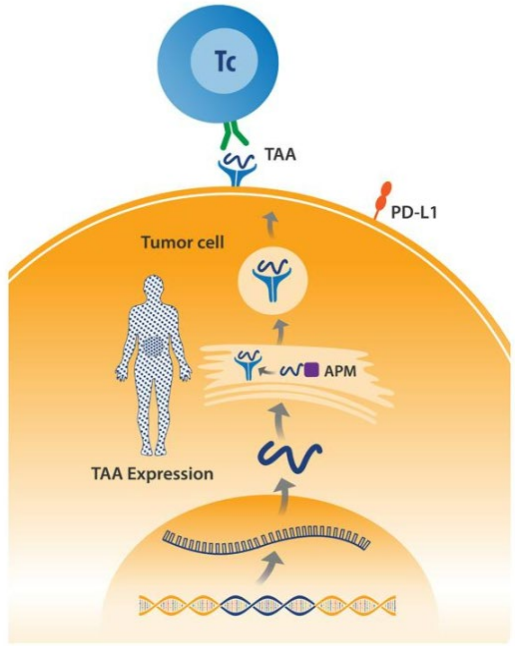
Multiple Important Milestones of PCV in Next 1-2 Years

Company	Indication	Clinical stage	Near-term milestone
moderna	Adjuvant Melanoma	Phase 3	Data readout in 2026
	Adjuvant NSCLC	Phase 3	Enrollment completion in 2025
	Adjuvant NSCLC post neoadjuvant treatment	Phase 3	Enrollment completion in 2025
	Renal Cell Carcinoma	Phase 2	Enrollment completion in 2025
	Bladder Cancer	Phase 2	Enrollment completion in 2025
	Cutaneous Squamous Cell Cancer	Phase 2	
BIONTECH	Adjuvant Colorectal Cancer	Phase 2	Clinical Readout beyond 2025
	Adjuvant Pancreatic Ductal Adenocarcinoma	Phase 2	Clinical Readout beyond 2026
	Muscle-Invasive Urothelial Cancer	Phase 2	Clinical Readout beyond 2026

mRNA Tumor Associated Antigen (TAA) Cancer Vaccine Program

EVEREST MEDICINES

EVM14: An Off-the-Shelf Tumor Associated Antigen (TAA) Vaccine



Overexpressed proteins, differentiation antigens	Cancer testis antigens	Target types
VARIABLE	GOOD	Tumor specificity
HIGH	LOW	Central tolerance
HIGH		Prevalence in multiple patients

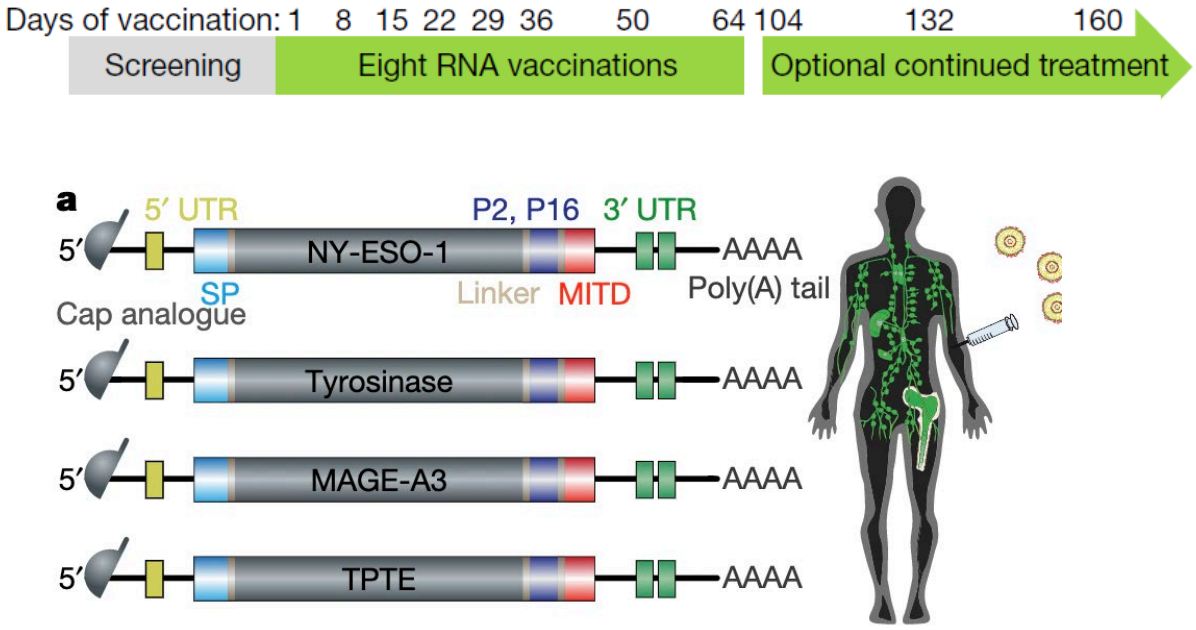
Advantages of TAA cancer vaccine

- Good tumor specificity (tumor vs. normal)
- More T cell epitopes and no HLA restriction
- Off-the-shelf, well suited for advanced disease
- Reduced manufacture costs (vs. PCV)
- Potential for multiple cancer indications (depending on TAA expression)

IND enabling studies completed, US IND submitted in February

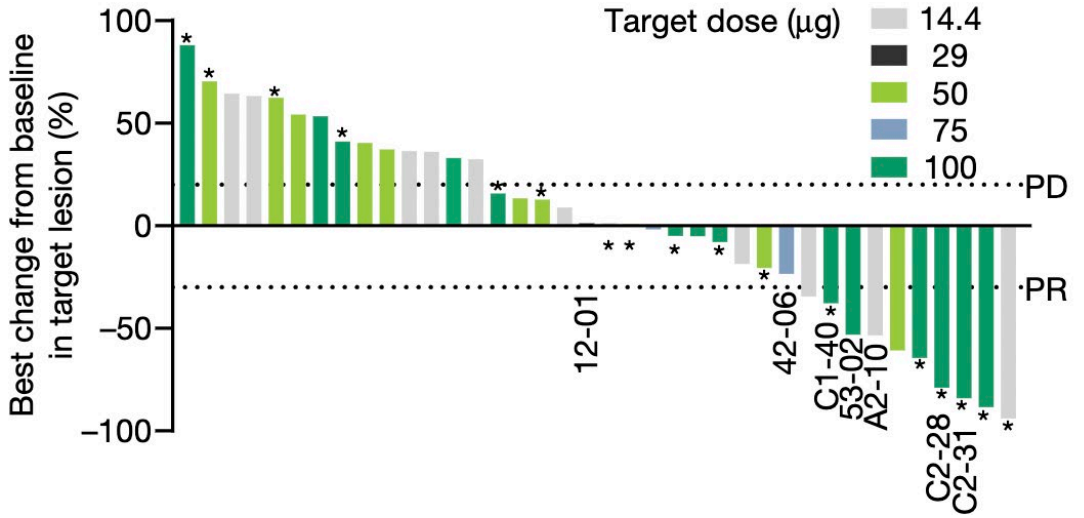
EVEREST MEDICINES

Promising Responses to a TAA mRNA Vaccine in a Phase 1 ICB-Relapsed Melanoma Trial



Advanced Melanoma
42 pts experienced CPI
35 pts had PD1&CTLA4

More than 90% of melanomas in patients express at least one of the four TAAs encoded in BNT111 (NY-ESO-1, MAGE-A3, tyrosinase, and TPTE).



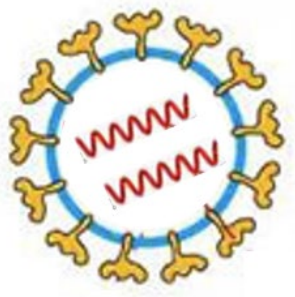
Cohort	ORR, %
Vaccine mono (30)	16
Vaccine + anti-PD1 (26)	35

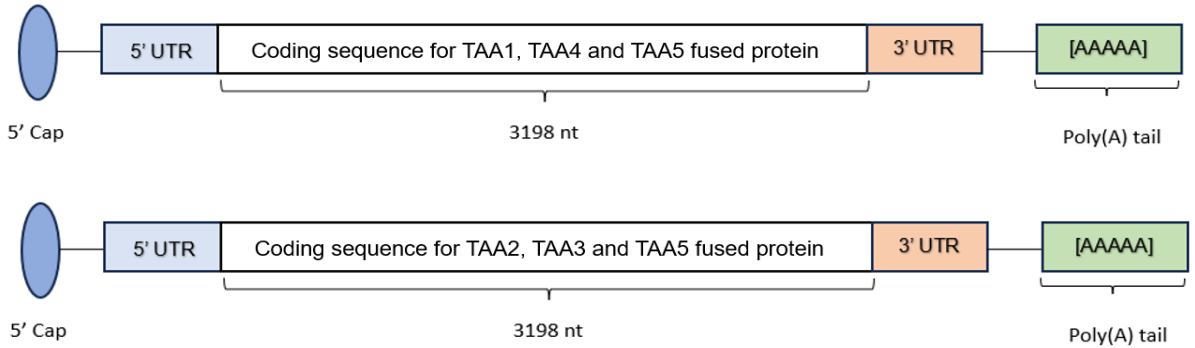
Sahin et al, Nature, 2020

EVEREST MEDICINES

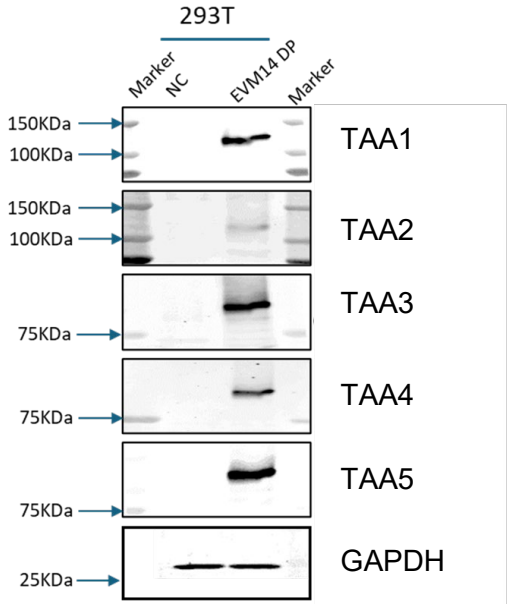
EVM14 is a TAA Vaccine Designed to Target 5 TAAs

EVM14 is a bi-valent vaccine designed to target 5 TAAs



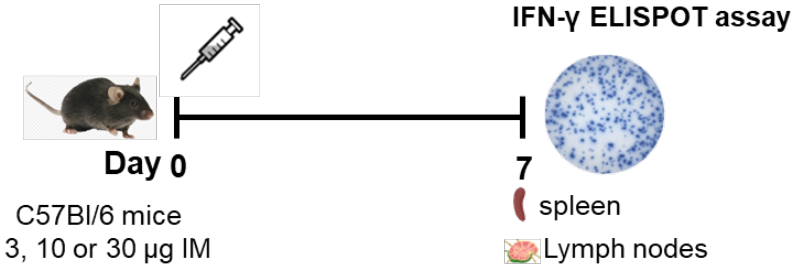


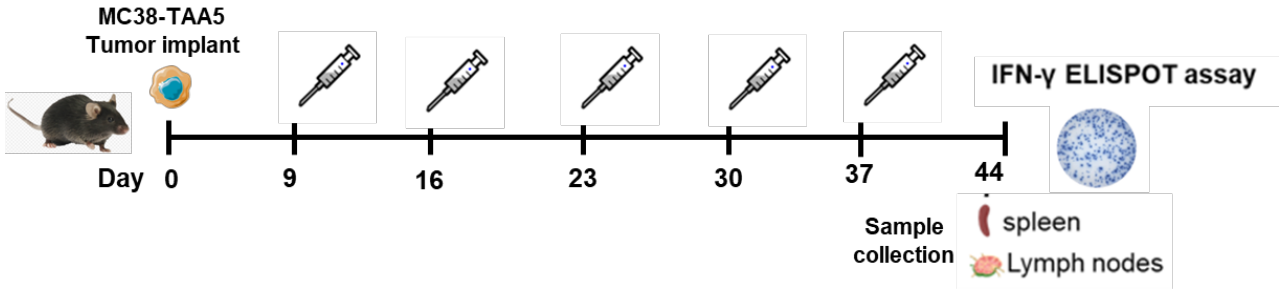
Good expression of EVM14 for all TAAs in 293T cells in vitro

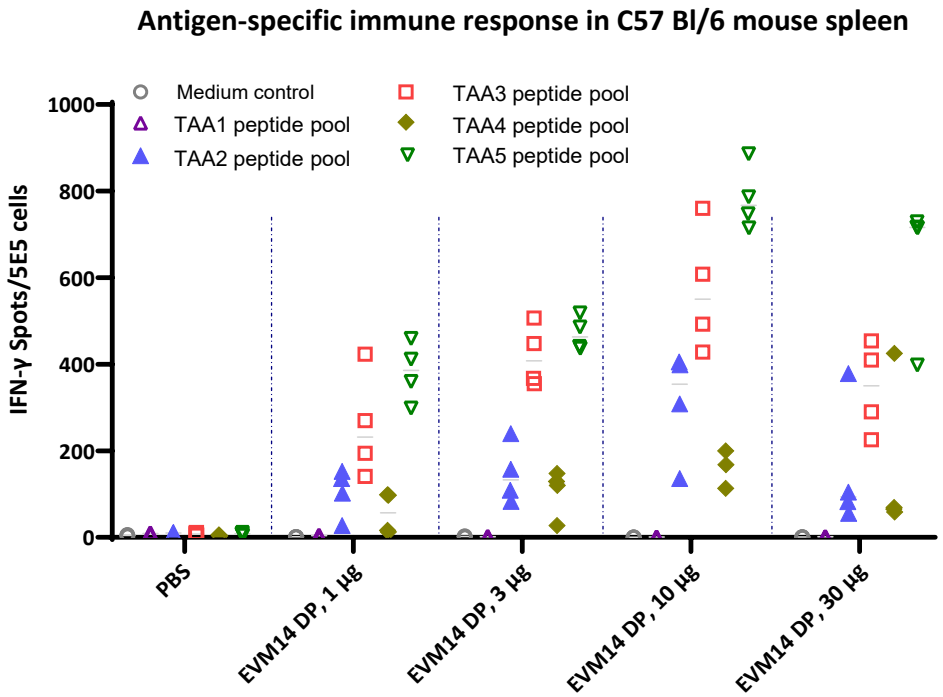


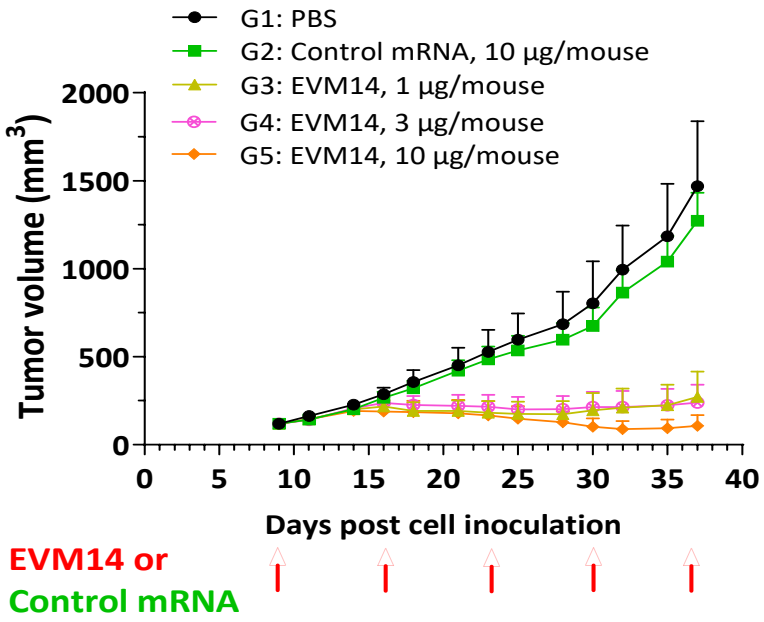
EVEREST MEDICINES

EVM14 Induced Dose-dependent Antigen-Specific Immune Response in C57Bl/6 Mice





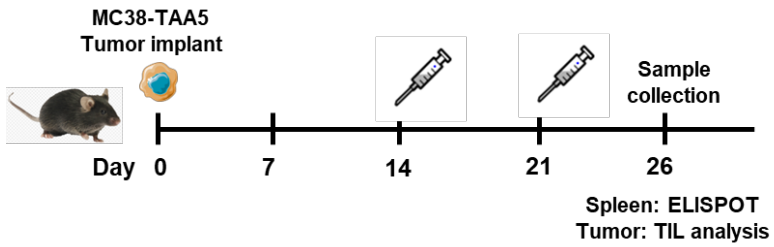




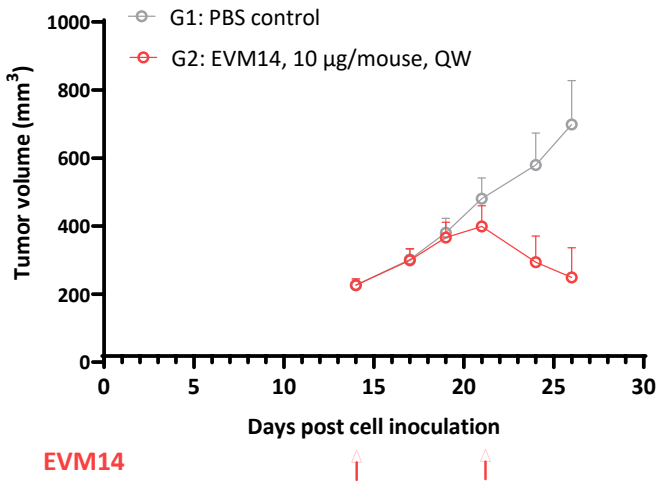
EVM14 vaccination induced dose-dependent antigen-specific immune response in C57Bl/6 mice, with maximal T cell response at 10 µg.

EVM14 vaccination leads to dose dependent anti-tumor efficacy in mouse syngeneic model

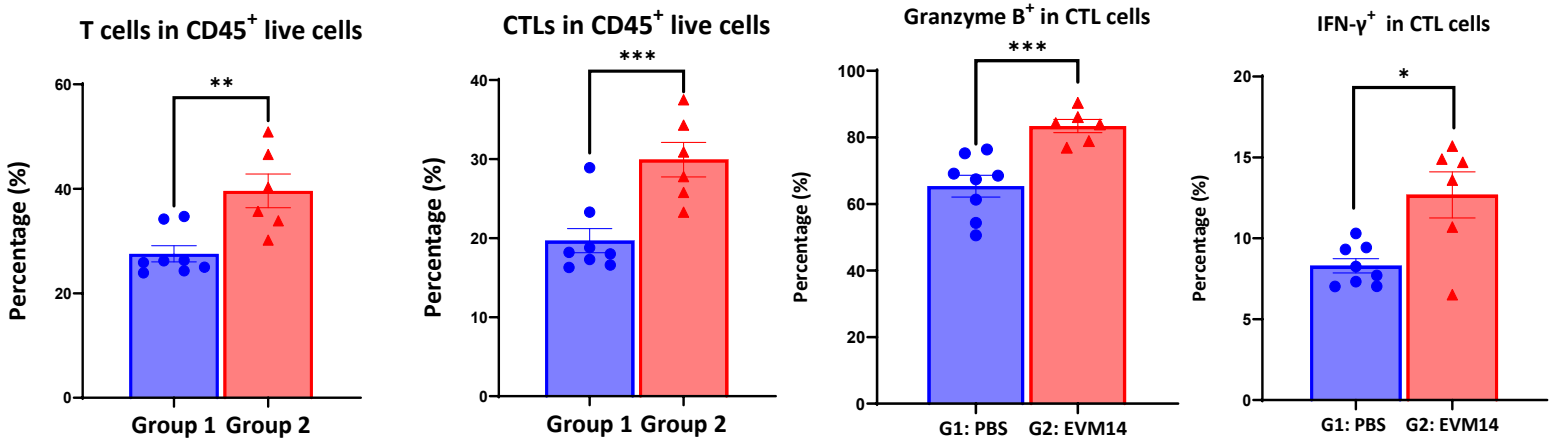
EVM14 Induced T Cell Infiltration and Activation in MC38-TAA5 Tumor Tissues



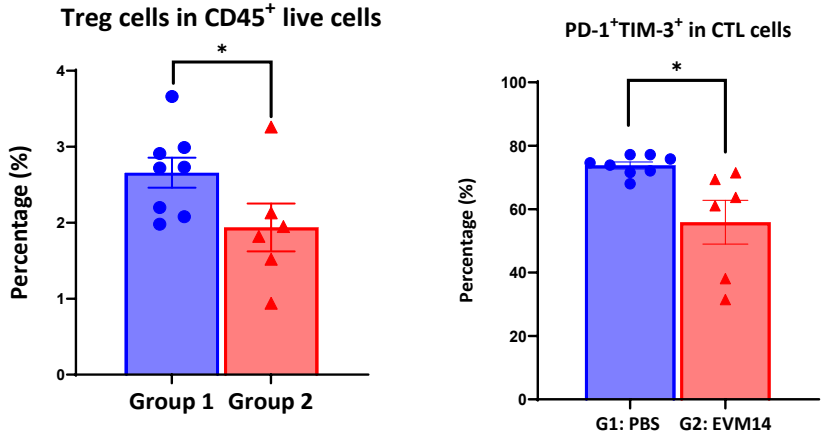
Two doses of EVM14 at 10 μg/mouse significantly inhibited tumor growth in MC38-TAA5 model.



Two doses of EVM14 significantly enhanced T cell infiltration into tumor tissues and increased CTL activation.

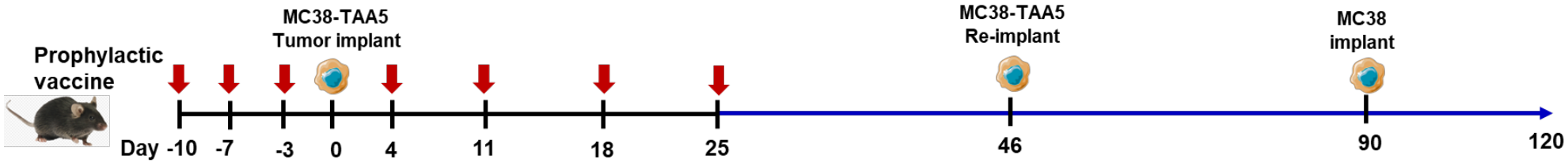


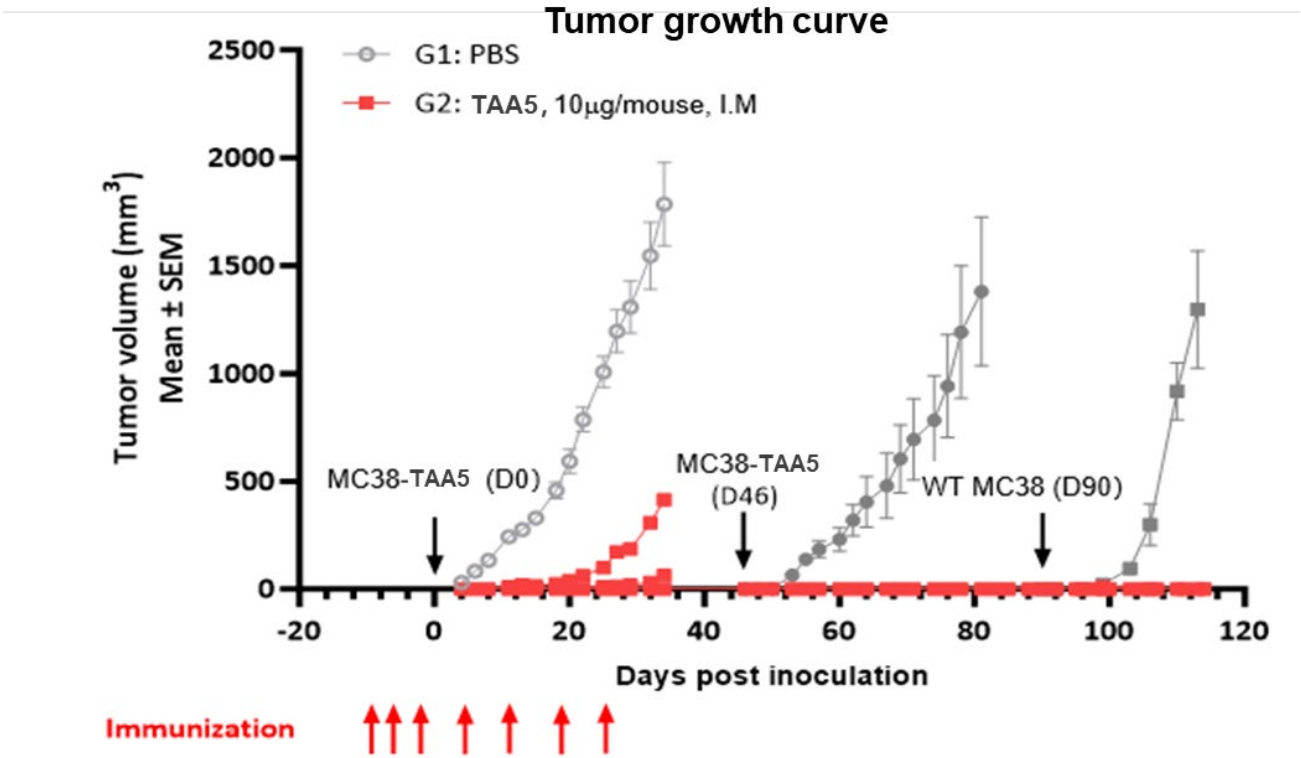
Two doses of EVM14 significantly decreased tumor-infiltration of Treg cells and CTL exhaustion.



EVEREST MEDICINES

TAA Cancer Vaccine Can Induce Immune Memory and Prevent Tumor Recurrence

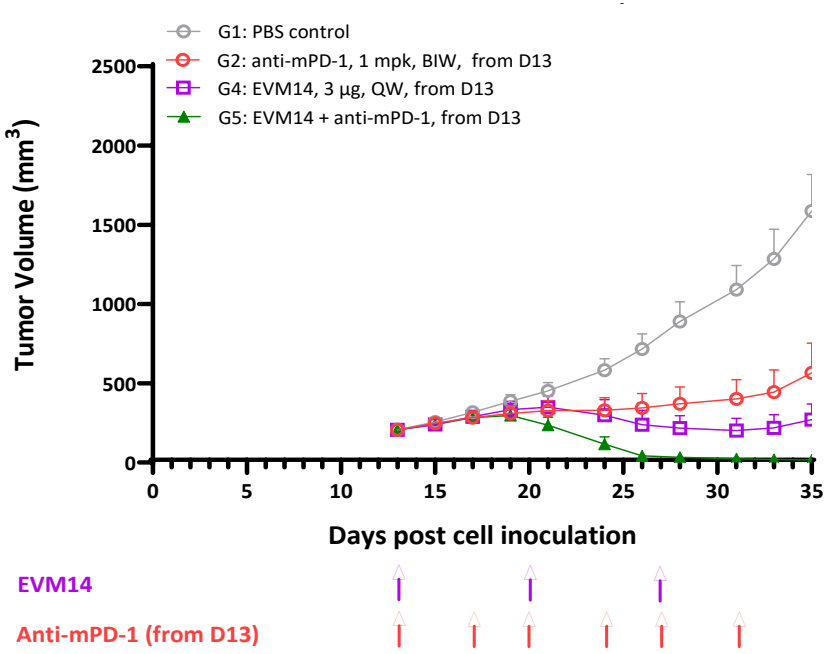




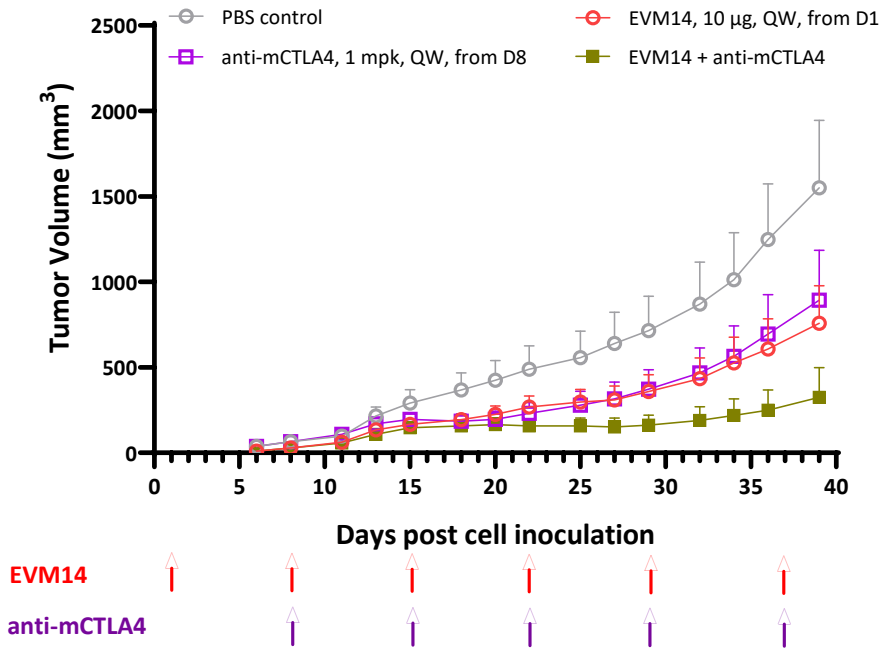
After EMV14 treatment, the majority of (13/15) mice saw complete tumor retraction. Tumor did not re-grow after re-introduction of MC38-TAA5 tumor cells or wild-type MC38 tumor cells.

Combination of EVM14 With Immune Checkpoint Inhibitors (ICIs) Significantly Enhanced Anti-tumor Activity

EVM14 and **anti-PD1 antibody** combination therapy



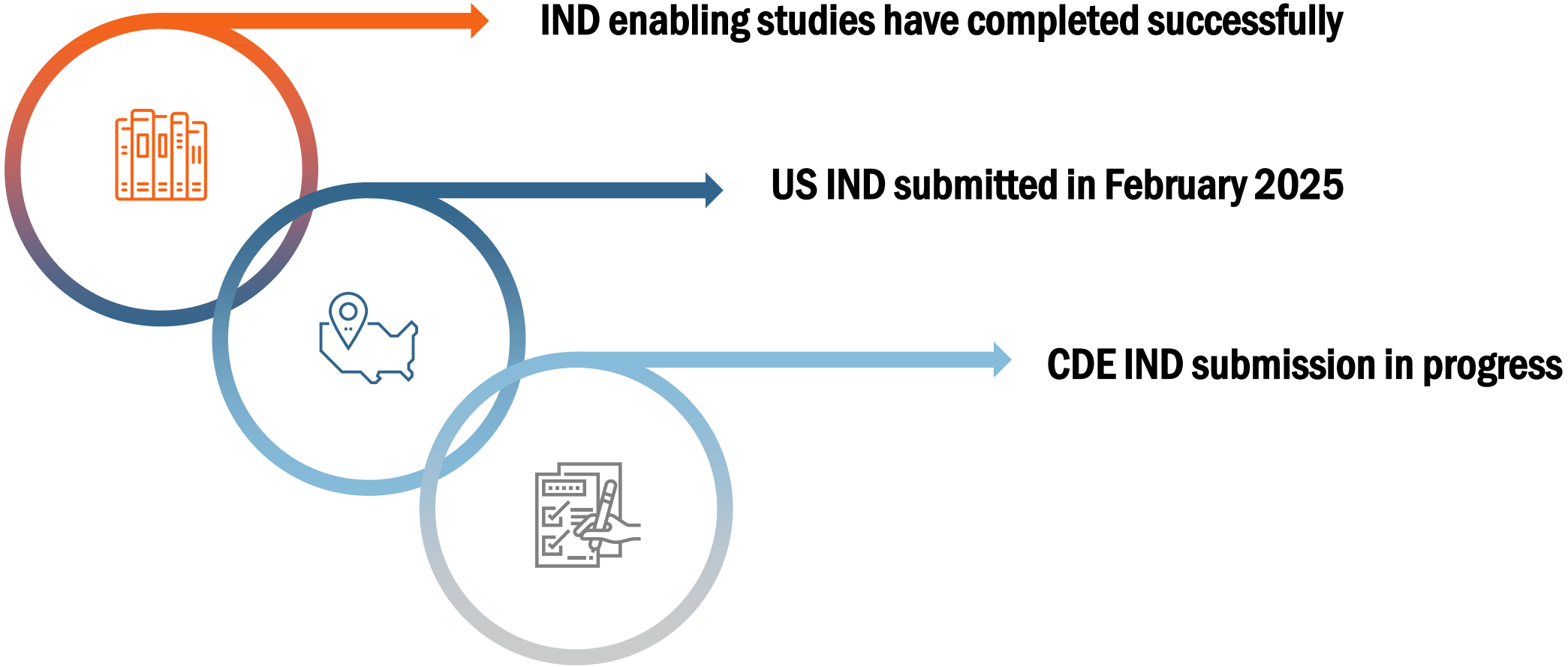
EVM14 and **anti-CTLA4 antibody** combination therapy



Combination of EVM14 with anti-PD1 antibody or anti-CTLA4 antibody significantly improved anti-tumor activity in preclinical models, supporting exploration of the combination in clinic

EVEREST MEDICINES

Recent Progresses of EVM14



IND enabling studies have completed successfully

US IND submitted in February 2025

CDE IND submission in progress

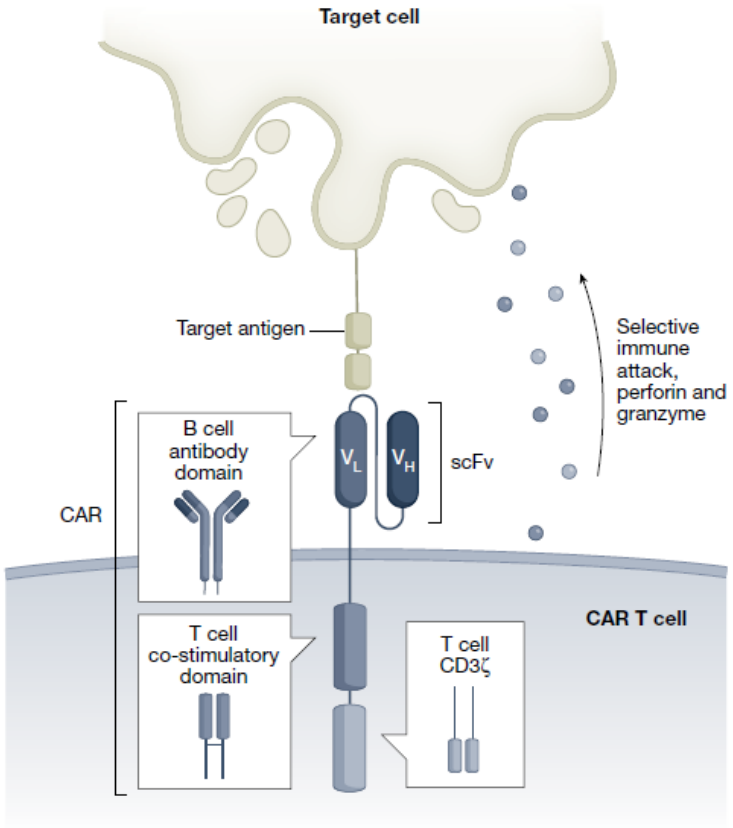
EVEREST MEDICINES

mRNA in-vivo CAR-T Program

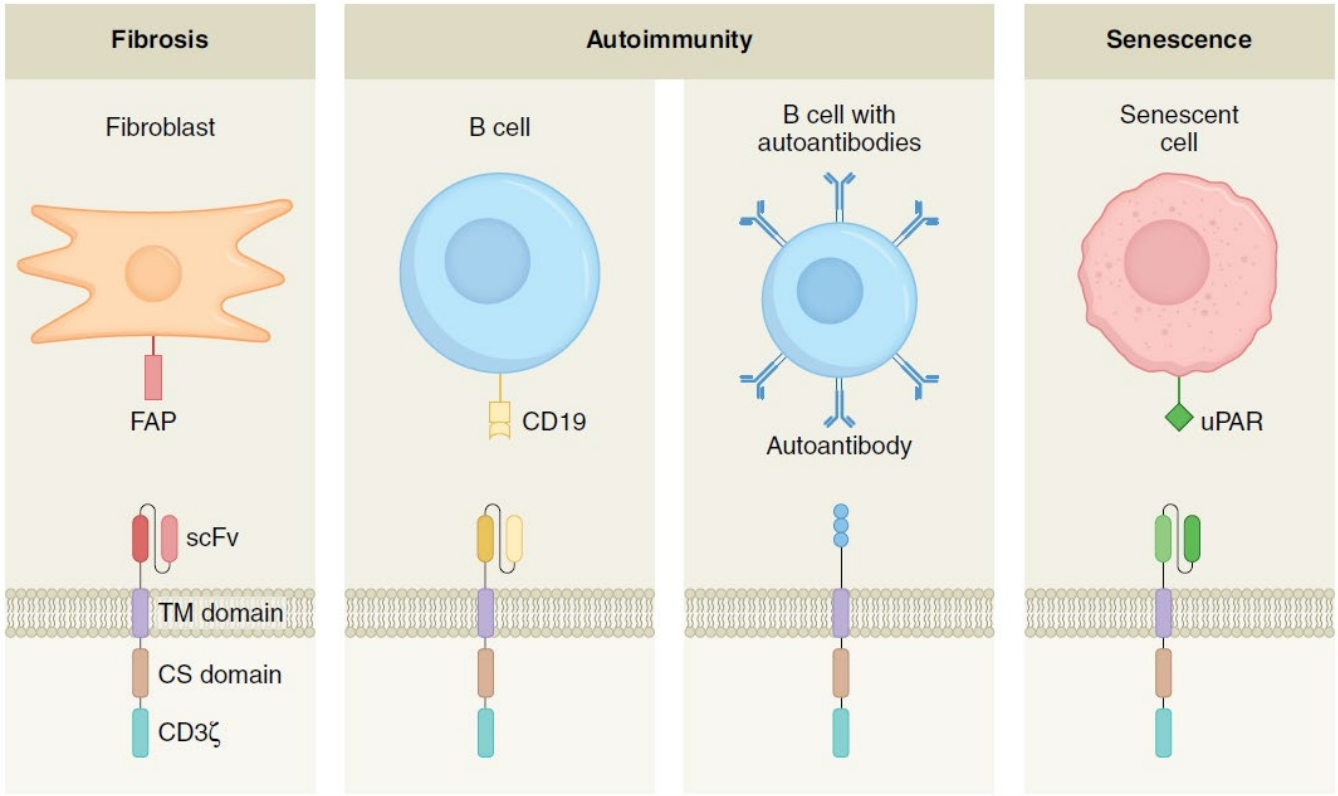
EVEREST MEDICINES

CAR-T Therapy Expands its Application Beyond Cancer

CAR-T working principle



New applications in other diseases



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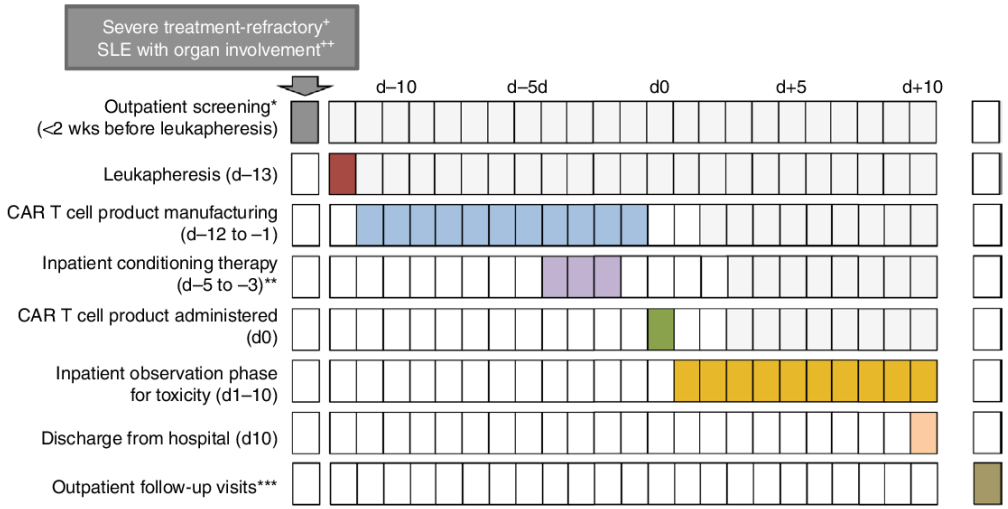
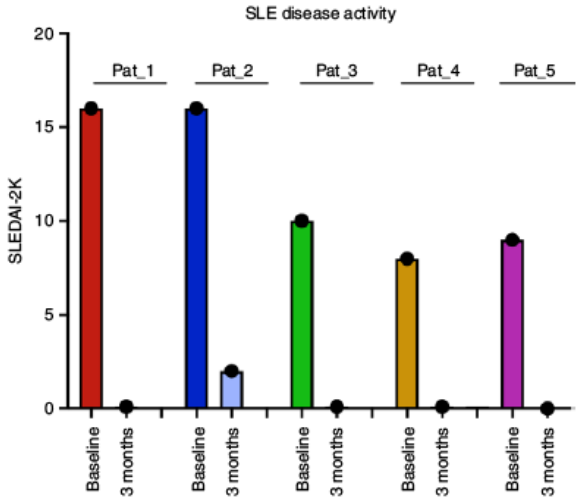
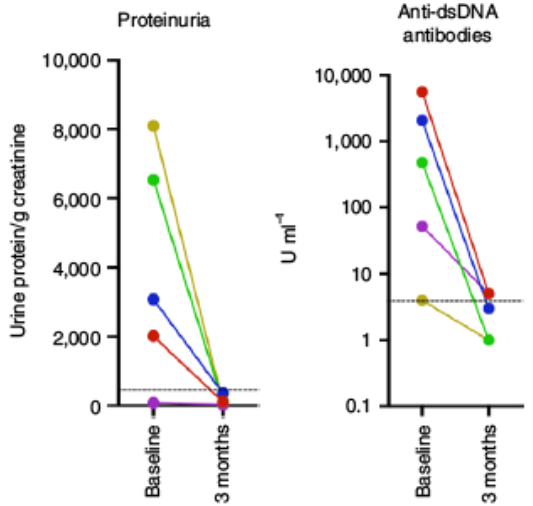
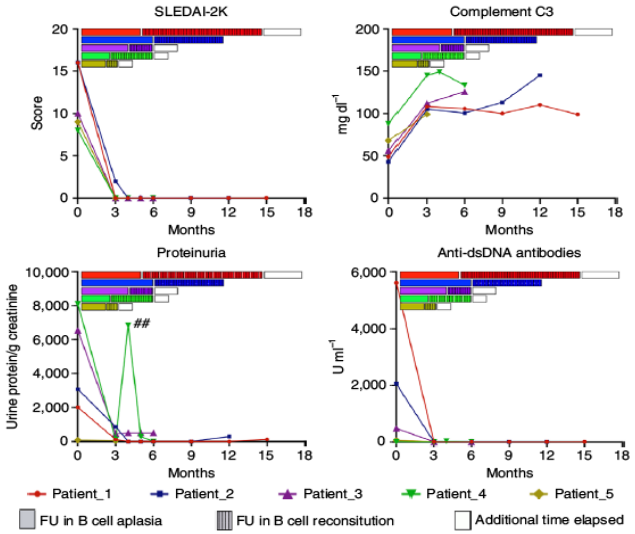
Success of Anti-CD19 CAR-T Therapy for Refractory Systemic Lupus Erythematosus







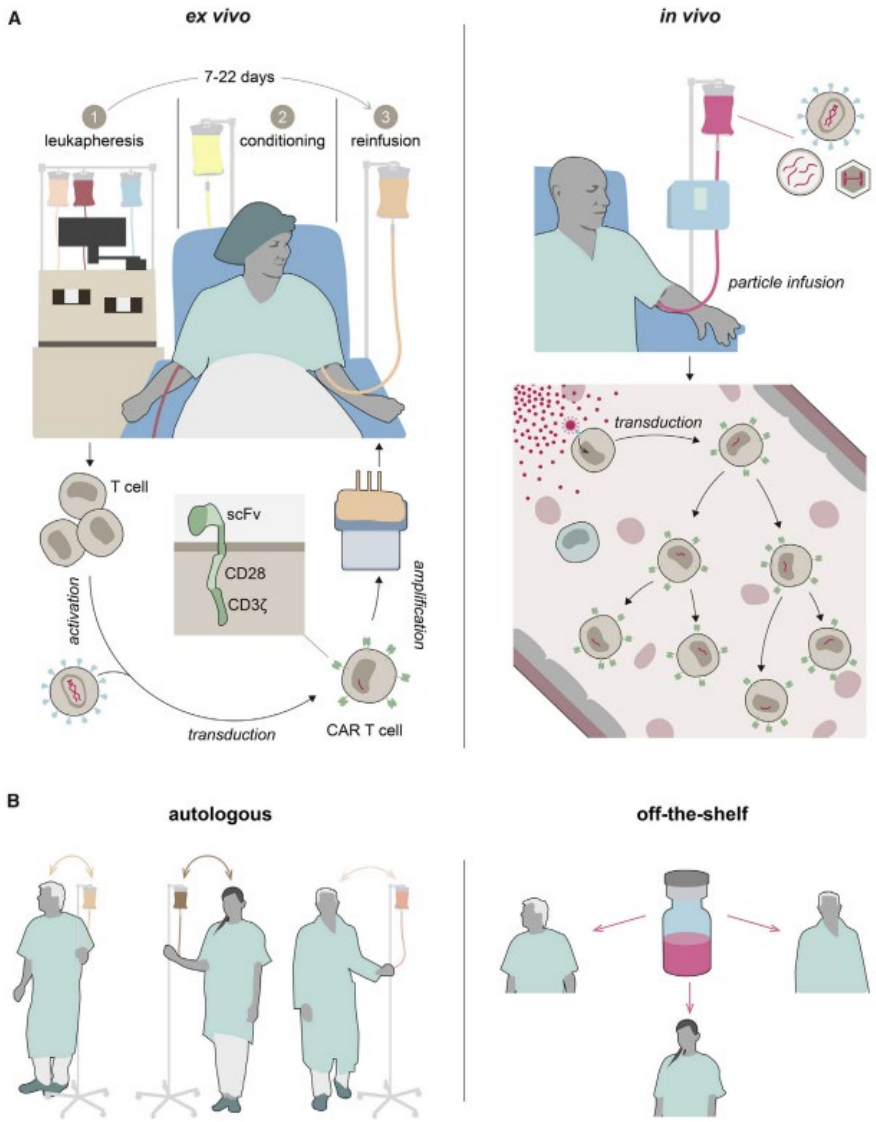


Key Findings:

- **No relapse (SLE drug free) in long term follow up** (5mo-17mo) despite B cell reconstitution around 4mo
- **"Re-set" the immune system**: Recurrent B cells were mostly naïve cells while lack of plasmablasts, memory B and activated memory B cells
- **Favorable safety profile**: No or only mild CRS; No ICANS (immune effector cell-associated neurotoxicity syndrome); No relevant hemodynamic changes were observed; No infection occurred in the phase of B cell aplasia; Fever was manageable by metamizole and tocilizumab

EVEREST MEDICINES

In vivo CAR-T Could Address Challenges Faced by Conventional CAR-T Therapy



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Autologous CAR-T Therapy

Disadvantages

- High cost of production
  Limited market access
- Requires lymphodepletion
  Increase safety risk
- Post-treatment
  hospitalization
- In vivo expansion leads to
  uncontrollable PK and PD
- Variable cell quality

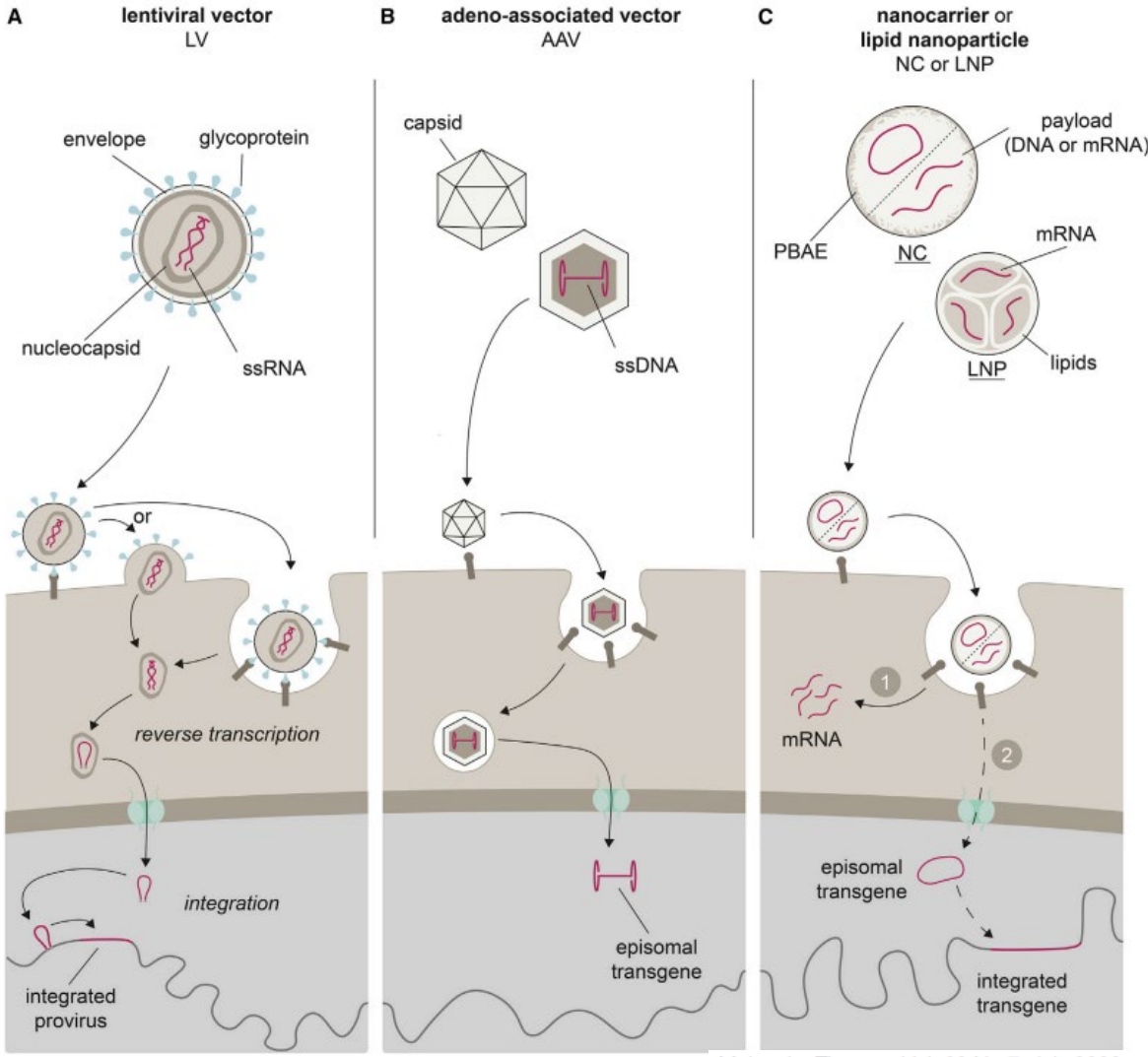
mRNA in vivo CAR-T

Advantages over autologous CAR-T Therapy

- Off-the-shelf
  Scalable
- No lymphodepletion
  conditioning
- Hospitalization may not be
  needed
- Tunable exposure
  Predictable PK/PD
- Cell free
  Controllable quality

EVEREST MEDICINES

Everest Uses mRNA/tLNP Platform for in vivo CAR Delivery



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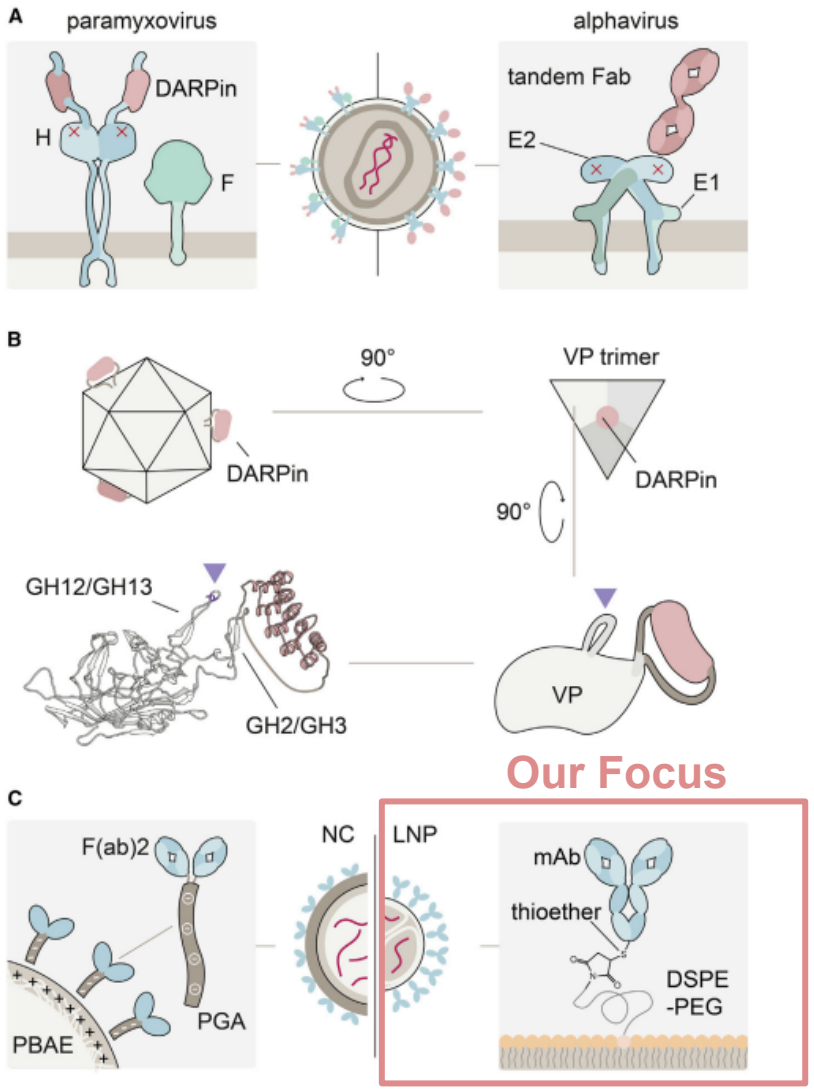
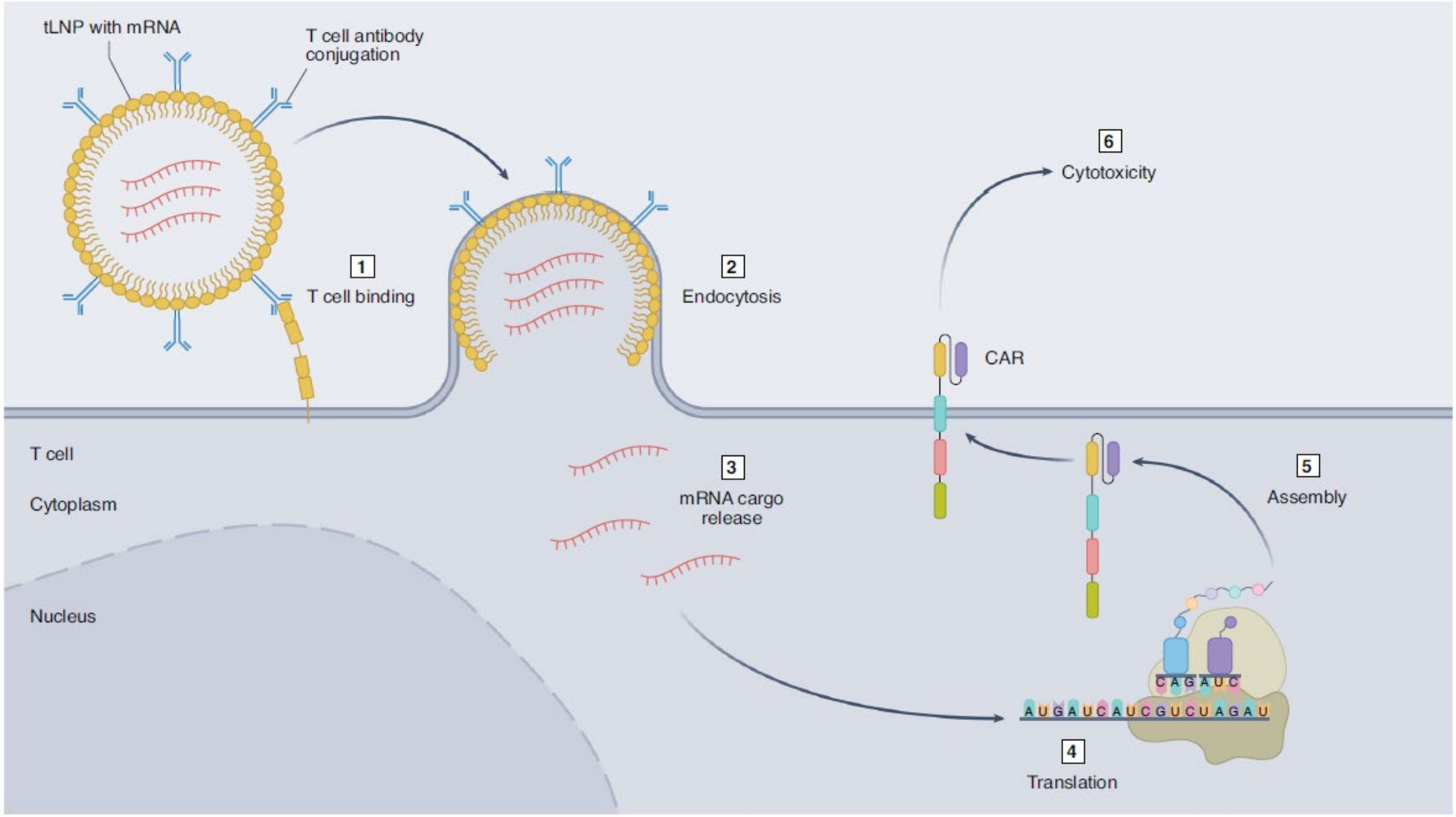


Our Focus

EVEREST MEDICINES

In vivo mRNA CAR-T Mechanism of Action



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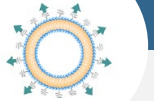
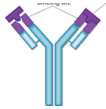
EVEREST MEDICINES

mRNA in vivo CAR-T Program Validated in Several Pre-clinical Models



Robust conjugation method has been developed to ensure consistent and high conjugation efficiency



Appropriate targeting moiety has been identified that lead to specific and high expression of CAR in T cells

Efficacy and target cell depletion have been achieved in humanized tumor models

T cell transfection and CAR expression have been achieved in non-human primate (NHP) model

EVEREST MEDICINES

2025 Catalysts for mRNA Platform

mRNA platform			
	Personalized Cancer vaccines	TAA cancer vaccines	In vivo CAR-T
Indication	Cancer	Cancer	Cancer /Autoimmune
Catalyst	Complete IIT study Phase1a part	IND approval in US and China	First pre-clinical candidate

Great potential for GLOBAL PARTNERSHIP

Q&A

EVEREST MEDICINES