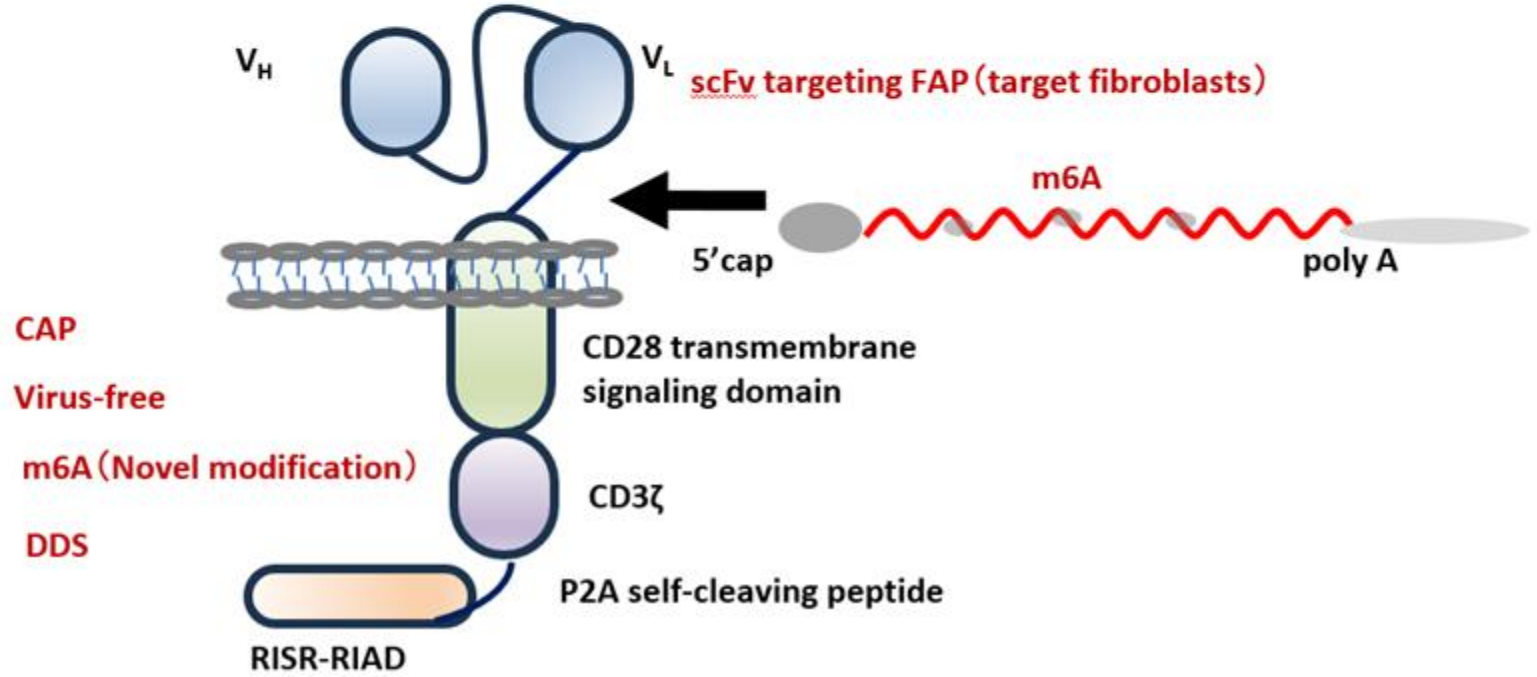
核酸

新規ポリマー基盤技術を活用した生体内誘導型CAR-T療法の開発

注射一本で、体の中にがん治療細胞を生み出す



疾患データサイエンス学
石井　秀始

- A One-Shot Polymer Platform for In Vivo Induction of CAR Immune Cells to Treat Fibrotic Diseases -

- 注射一本で“体内CAR細胞”を誘導する新規ポリマー技術による線維化疾患治療プラットフォーム -

大阪大学 THE UNIVERSITY OF OSAKA

The University of Osaka

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Institute of SCIENCE TOKYO

Institute of Science Tokyo

Yutaka Miura

Executive Summary

Research Objective

To develop an in vivo–induced FAP m^{6}A CAR-T therapy enabled by a polymer-based DDS, addressing stromal barriers in solid tumors and advancing a scalable RNA-engineered cell therapy platform.

Current R&D Stage

Demonstrated >1,000-animal in vivo validation, including complete regression of fibroblast-rich lesions and durable immune memory.
GMP-equivalent polymer formulation completed; GMP-grade LNP/RNA preparation ongoing.

Mechanism of Action / Modality

Modality: Virus-free, m^{6}A-modified CAR mRNA delivered by **next-generation polybetaine DDS**.
MoA: Transient in vivo reprogramming of patient T cells into FAP-CAR-T cells after intravenous delivery; selective depletion of CAFs in acidic fibrotic niches.
Biological Effects: Reversal of immune exclusion via CAF elimination, antigen spreading and immune memory formation, transient CAR expression (5–7 days) permitting safe, repeat dosing

Target Diseases

Fibrosis-dominant, immune-excluded solid tumors: **Immune, inflammation and fibrosis-based diseases, such as early-stages / precancerous lesions of cholangiocarcinoma**, **pancreatic cancer**, **colorectal cancer**
Early-stage / precancerous lesions where stromal transformation precedes tumor expansion.

Competitive Advantages Over Existing Therapies

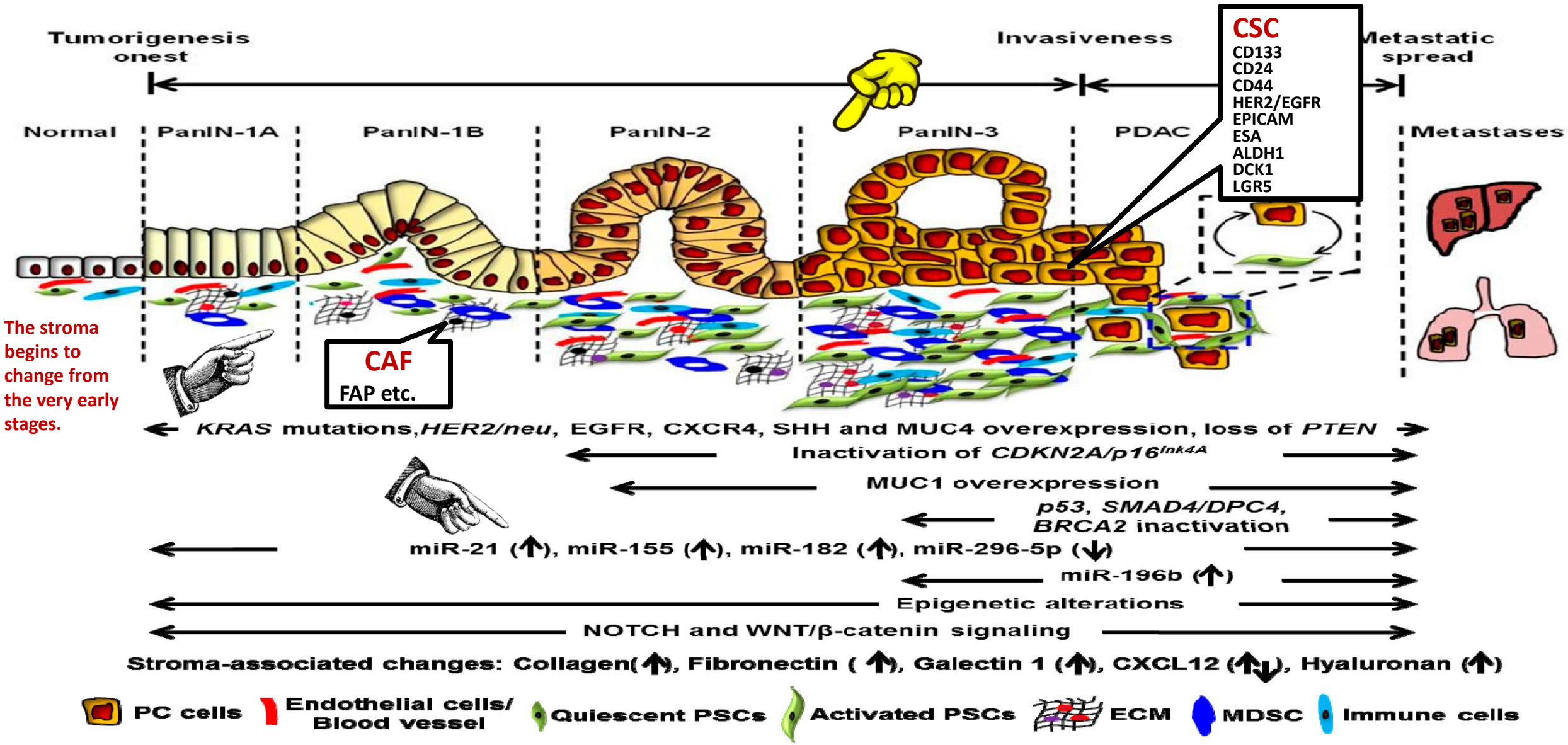
- Breakthrough DDS (Polybetaine): Ultra-low immunogenicity, PEG-free, minimal liver tropism; suited for repeat dosing (unlike LNP).
- Superior Translation Efficiency: 1.8× mRNA translation vs standard LNP; one-third interferon response.
- Solid Tumor Barrier Breakthrough: Only existing CAR modality directly depleting CAFs to reconstruct an immune-permissive microenvironment.

Desired Collaboration with Industry Partners

Co-development for FIH: Support GMP-grade polymer/LNP/RNA manufacturing. Joint execution of GLP toxicity studies and regulatory strategy (PMDA/FDA/EMA).
Strategic Partnership for Global Expansion: Build a co-owned RNA/DDS platform applicable to multiple antigens and diseases. Joint development of companion diagnostics and early-detection programs.
Commercialization & Market Strategy: Co-create a global first-in-class in vivo CAR-T pipeline. Develop integrated diagnostic–therapeutic products for precision RNA medicine.
Optional Milestone/Revenue-Sharing Structure: Early investment to secure exclusive licensing options for the FAP × m^{6}A-CART program and derivative pipelines.

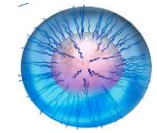
Backgrounds (1)

Chronic fibrosis of the liver, bile ducts, and pancreas can lead to various intractable diseases.

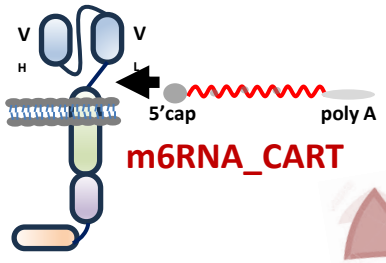


Backgrounds (2)

Fibrosis induces a low-pH microenvironment. If drugs can be delivered early using a breakthrough DDS, fibrosis can be directly targeted and treated.

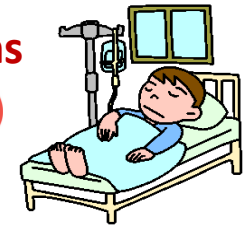


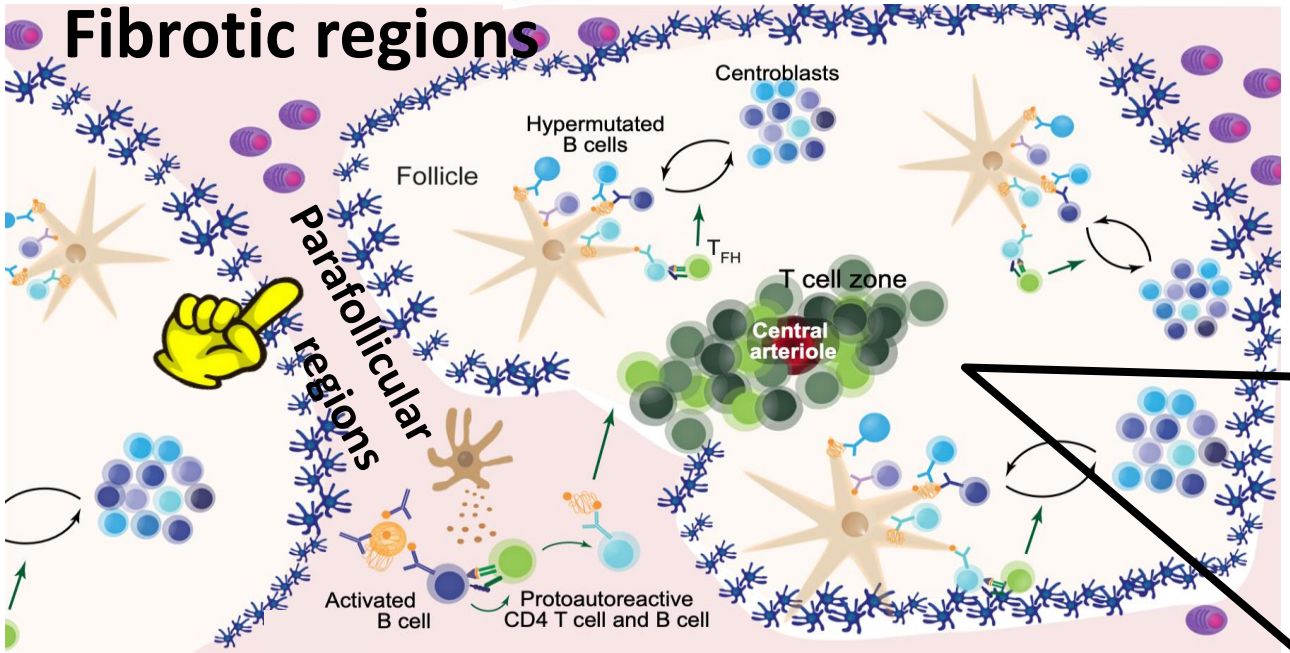
Novel DDS



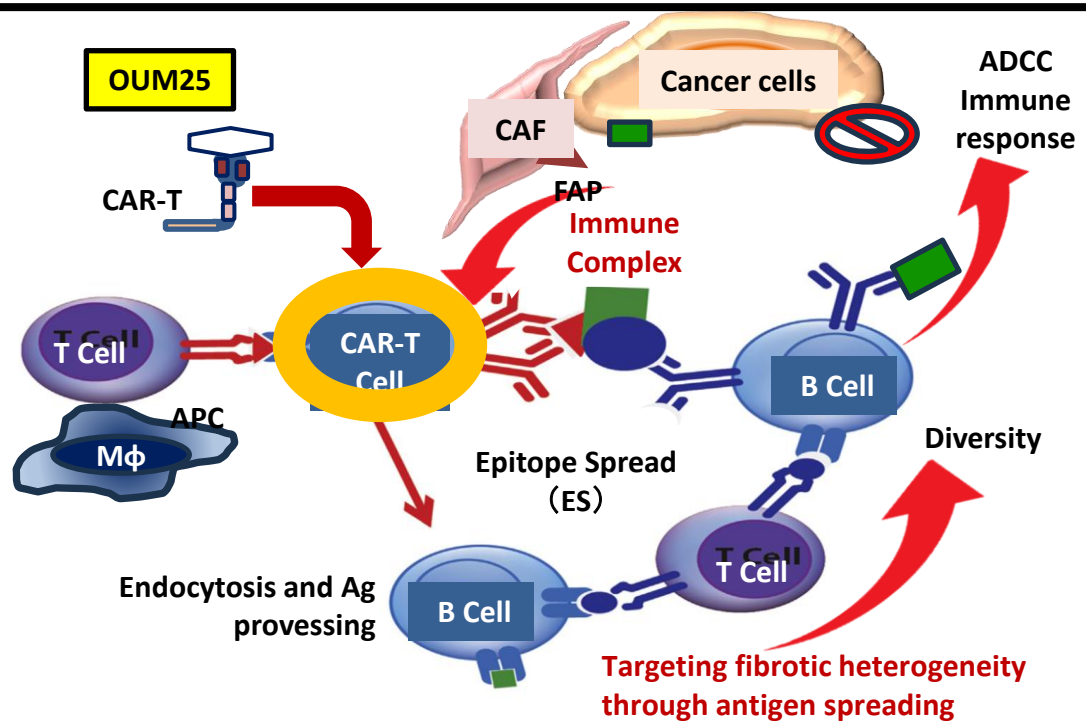
m6RNA_CART

One Shot Administrations





The extrafollicular regions of tertiary lymphoid structures (TLS), characterized by a relatively acidic environment (pH ~6.5), function as a niche for the deletion of autoreactive clones, phagocytosis-mediated antigen transfer and processing between macrophages and T cells, and the facilitation of antigen amplification.（Nature Communications.14:6941,2023）。



Through B cell reprogramming, m6RNA_CAR-T gains an additional layer of specificity that relies on antigen recognition via the BCR-encoded single-chain antibody (Fab) in addition to MHCII/TCR-dependent interactions, allowing for highly specific antitumor activity.

T cells reprogrammed into a B cell–like state gain antigen-processing functions akin to those of B cells and macrophages. By fragmenting and presenting complexes such as the FAP antigen bound to Fab, they facilitate the induction of "antigen amplification."（Immunol. Letter. 163,56–68,2015）。

Targeted Goal

Clinical Product Vision (Ultimate Goal): To develop the world's first FAP × m6RNA_CAR-T therapy, delivered via a low-pH–responsive polybetain polymer–based DDS platform, capable of overcoming the key obstacles posed by fibrosis-related disorders in the liver, biliary tract, and pancreas.

TPP (Target Product Profile)

Item	Content
Target Disease / Condition	Difficult-to-treat solid tumors in which fibrotic regions, even more CAFs (cancer-associated fibroblasts) form a high-density immune-excluded environment (e.g., cholangiocarcinoma, pancreatic cancer), especially at early stages (precancerous lesions)
Administration & Safety	Intravenous administration, basic schedule of 4 doses every other day, transient CAR expression for 5–7 days. No risk of gene insertion, incidence of CRS Grade ≥3 <10%, repeat dosing possible
Gene & Cells	Target: FAP (CAF-specific tumor antigen) / Gene: m^{6}A-modified CAR RNA / Cells: transient reprogramming of patient's own peripheral T cells in vivo
Background & Direction	To overcome the biggest barrier in solid tumor immunotherapy—the stromal barrier—developed the world's first FAP × m6A-modified RNA-LNP in vivo CAR-T. Features: safe, low-cost, rapid manufacturing. Aiming for practical application around 2030 as a NOVEL solid tumor immunotherapy platform

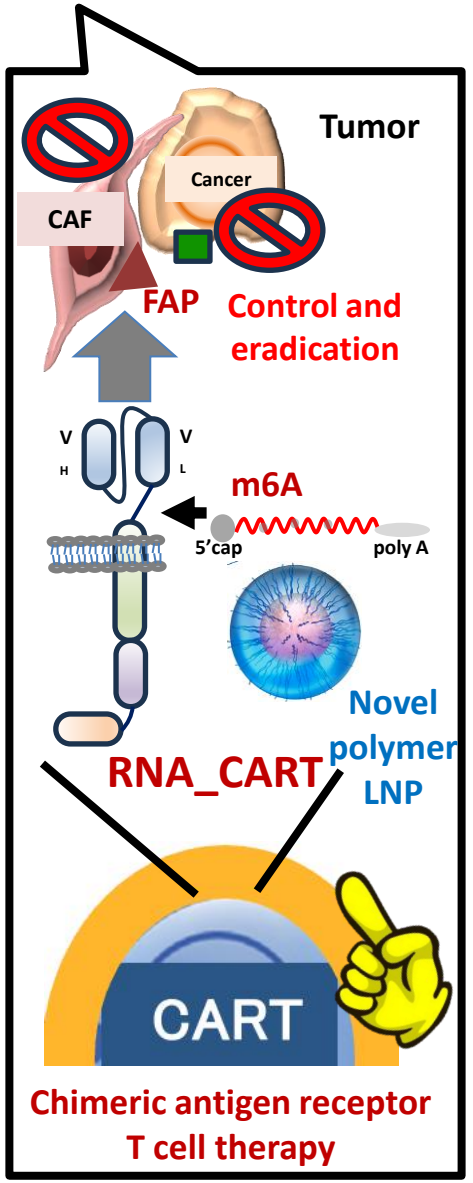
"CAF modulation as a starting point for solid tumor therapy"

In vivo administration of FAP-targeted m6A-modified RNA via LNPs transiently programs T cells into CAR-T cells targeting CAFs.

Reconstructs the immune-excluded microenvironment of solid tumors.

Transient expression ensures safety and allows for repeated dosing.

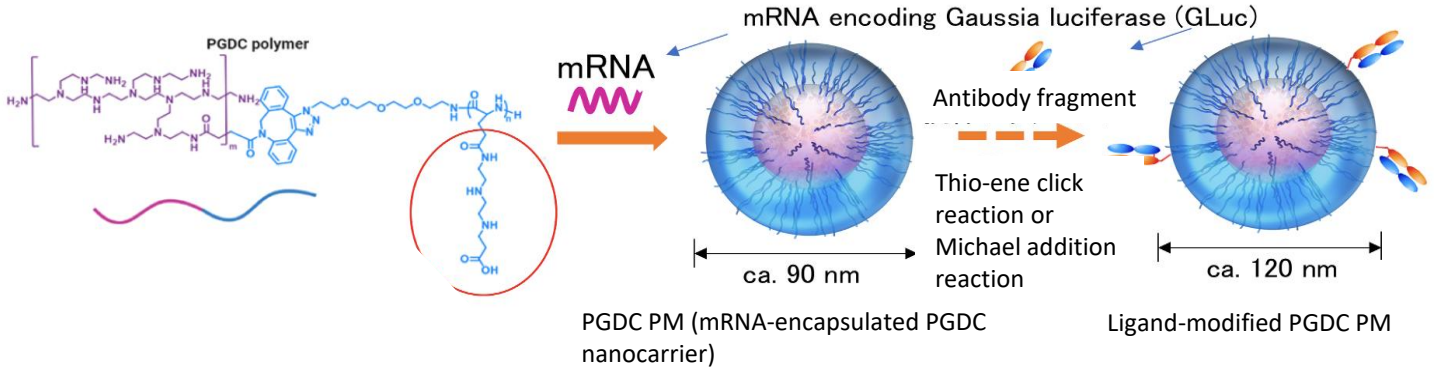
FAP: Fibroblast Activated Protein



Polymer-Enabled CARTs: Technology Overview

- **Non-viral, polymer-based delivery with high safety and manufacturability**
- **Transient, controllable activity tailored to fibrotic and inflammatory microenvironments**

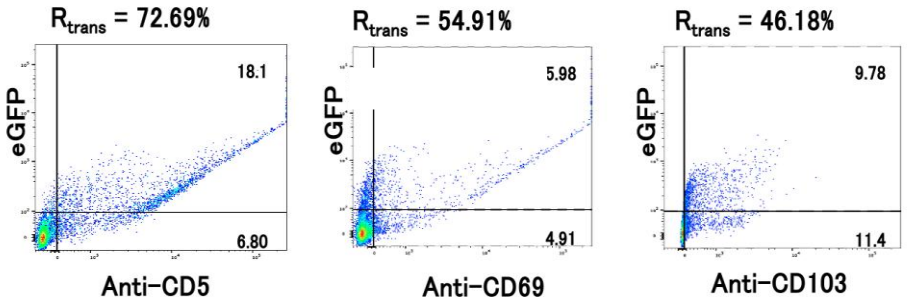
A Novel, RNA-Optimized Polymer Architecture



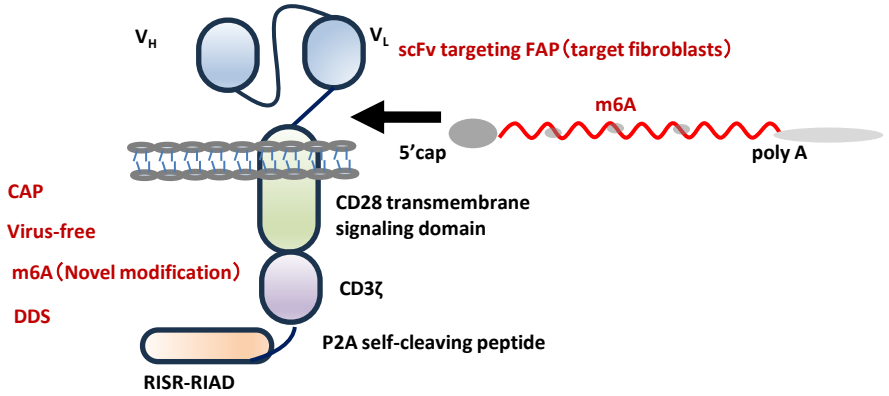
PGDC PM (mRNA-encapsulated PGDC nanocarrier)

Ligand-modified PGDC PM

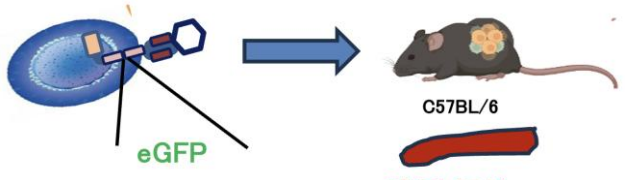
Superior Delivery Efficiency



A Proprietary Engineered CAR Architecture



>1,000-Animal In Vivo Validation



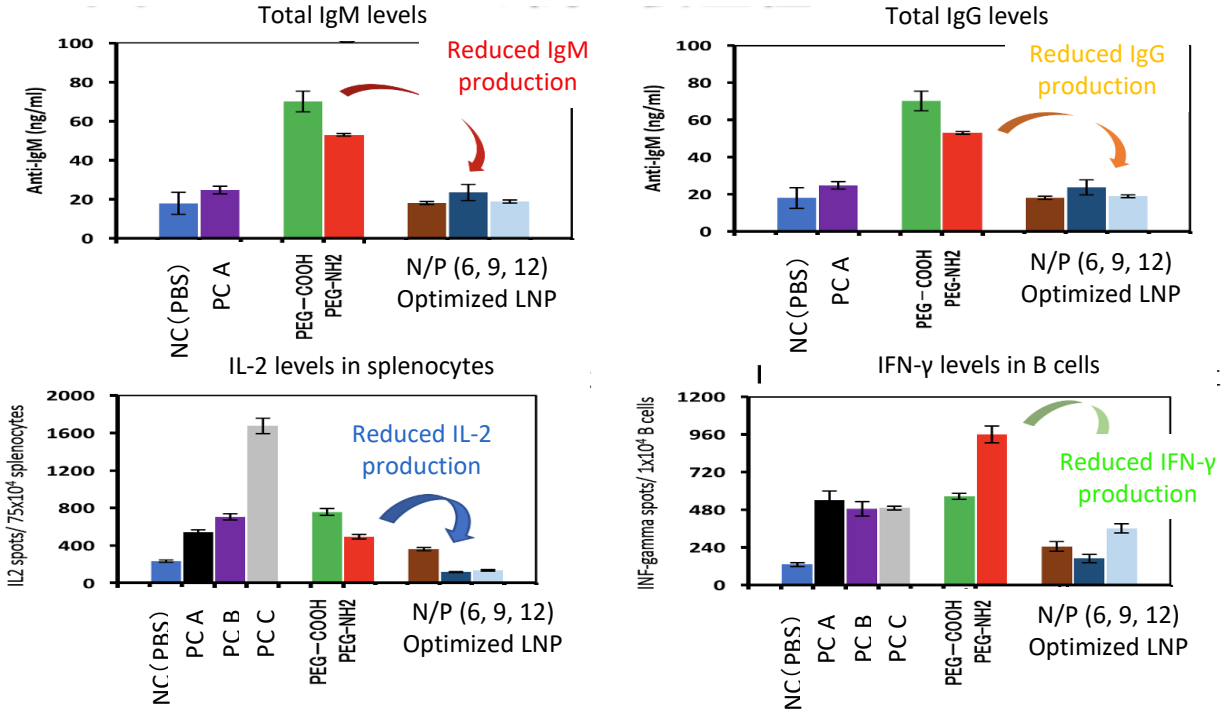
Transformative Technologies to Overcome Fibrotic Diseases: Toward Real-World Implementation

A high-performance polymer platform for mRNA Medicine

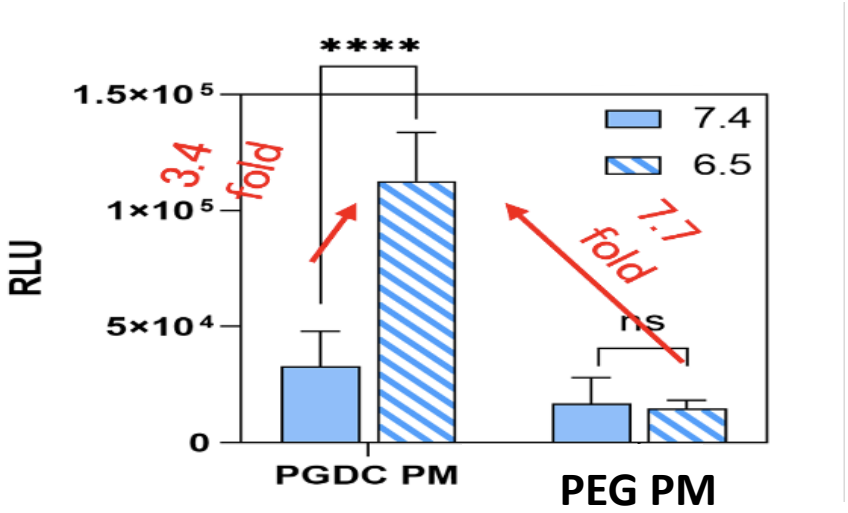
Low Immunogenicity + High Translation Efficiency

- **Safe, non-viral polymer delivery with superior manufacturability**
- **Fully scalable, off-the-shelf design** for widespread clinical deployment

Low Immunogenicity (Safety): One-Third IFN Response



High Translation Efficiency (Efficacy): 1.8× Increase

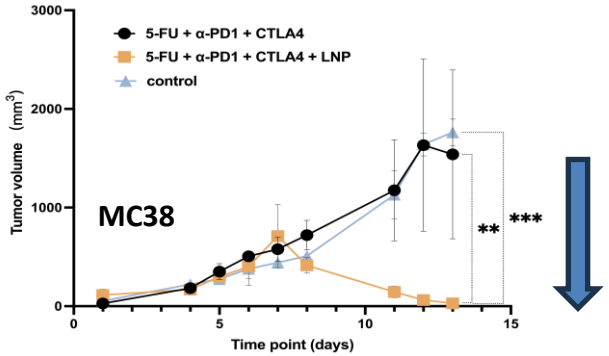


Our novel polymer platform delivers exceptional performance that can be broadly applied across diverse RNA therapeutics.

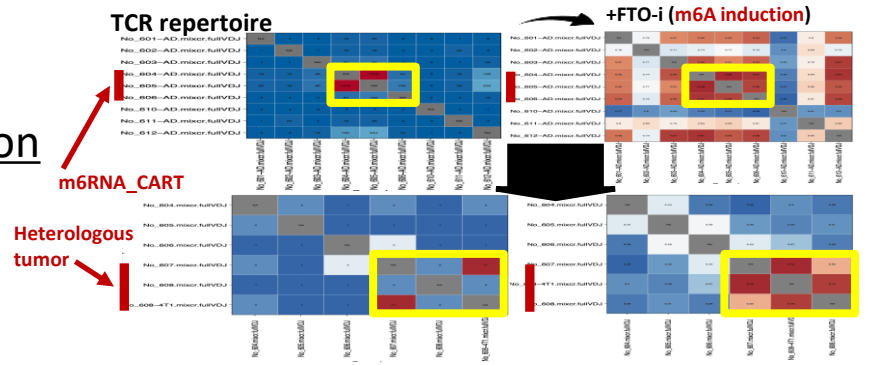
Polymer-Enabled CARTs: Eradicating Fibroblasts and Establishing Immune Memory in Animal Models

- **Shrinks fibroblast masses and prevents regrowth for >90 days**
- **RNA-engineered immune memory with IL-7–driven antigen expansion**
- **No detectable toxicity in normal tissues (mouse)**

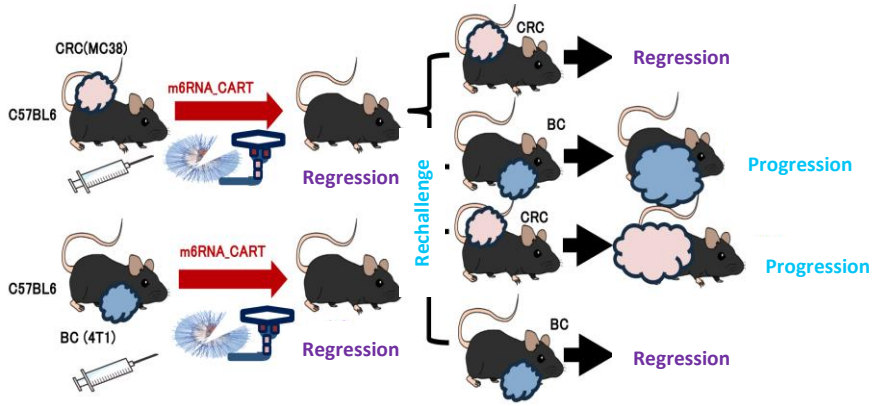
Achieved complete eradication of fibroblast-rich lesions

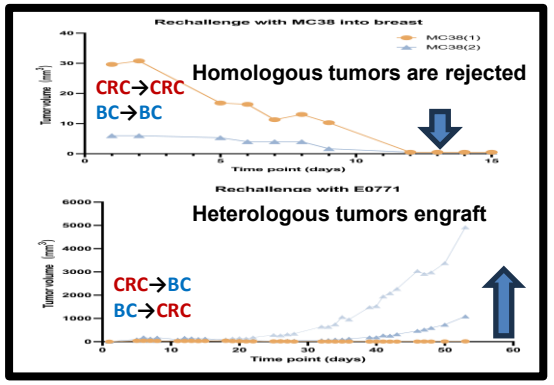


TCR repertoire analysis revealed clear antigen-driven immune expansion



Complete eradication enabled by antigen-specific immune memory—unachievable with nonspecific immunity





Induction of immunological memory

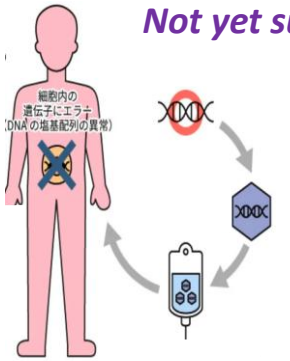
A breakthrough medical technology that fully controls fibrosis and eliminates the risk of recurrence.

Unmatched Differentiation and Clear Competitive Advantage

In vivo modality (transiently reprograms T cells within the body)

CRISPR Genome Editing

200 billion USD globally



Not yet successful in clinical practice

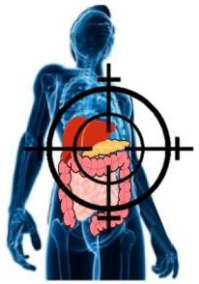
Hematologic malignancies (leukemia/lymphoma)

Evolution of the Operational Platform

RNA_CAR-T

This proprietary technology platform

Multiple dosing
Estimated drug price: 30,000 USD



A technological axis that delivers orders-of-magnitude improvements in manufacturing cost, speed, and safety

1,000 billion USD globally

Blue Ocean

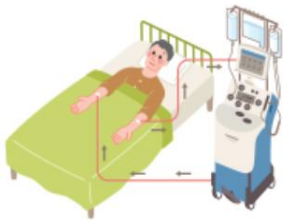
Expansion of Tumor Targets

Solid tumors, including pancreatic, biliary tract, and colorectal cancers

Red Ocean

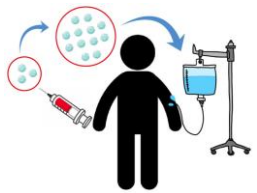
70 billion USD globally

Viral CAR-T



Single-dose administration
·Estimated drug price: 300,000USD

Not yet successful in clinical practice



Adoptive cell therapy

100 billion USD globally

Larger Market / Untapped Opportunity

Ex vivo modality (modifies and expands T cells outside the body)

Benchmark Analysis Against Three Competing Products

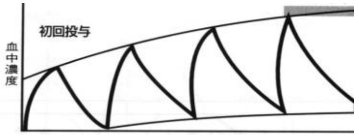
Factor	This proprietary technology platform（Polybetain DDS × m⁶A × FAP-CAR）	United Immunity（Pullulan, polysaccharide DDS）	Capstan Therapeutics（LNP × in-vivo CAR）	Strand Therapeutics（Synthetic mRNA × LNP）
DDS	**Polybetaines (PEG-Free, Ultra-Low Immunogenicity)**	Pullulan, a polysaccharide	LNP（PEG）	LNP（PEGylated）
Immunogenicity	**Ultra-Low: Suitable for Repeat Administration**	Low–Moderate	Moderate-High（PEG Issue）	Moderate-High
Liver tropism	**Low**	Moderate	High（Major Vulnerability）	High
RNA translation efficiency	**High（m⁶A × Polybetain）**	Moderate	High	Moderate-High
Key target cells	**T Cell・CAF（FAP⁺）**	macrophages／DC	T cell	Tumor cells
Application to solid tumors	**◎（Overcoming Immune Exclusion via CAF Depletion）**	△ (Immune Activation Only)	△ (Difficult to Reach / Deliver)	○ (Tumor-Specific)
Early-Stage Risk Management	**Precision Preventive Medicine（CDX＋DDS for CAR-RNA）**	△	×	×
Overall Competitiveness	★★★★★	★★	★★★	★★★

Only this platform can break the “solid tumor barrier” by targeting CAFs.
Only this platform offers a DDS (polybetaine) that goes beyond the post-LNP/PEG era.
Only this platform integrates diagnostics (m⁶A CDX) and therapeutics (RNA CTX) seamlessly.

m6A-CART Safety: Strategic Priorities from Preclinical Studies to Clinical Translation

① Safety-Optimized Dosing Design (Stepwise Dosing, Frequency, and Interval) [MRCPH]

Objective: Proactively mitigate “first-dose reactions and cumulative risk” associated with intravenous LNP administration.
Strategy:
Initial Dose: 10–20% of total dose → monitor → administer remaining dose (stepwise dosing).
Number of Doses: Up to 4 doses on alternate days (treatment completed before antibody induction).
Interval: 48 hours to minimize immune response.
Schedule: Dosing on **Day 0, Day 2, Day 4, Day 6**.



peak concentration
therapeutic range
trough concentration

② Safety Monitoring Panel (Mandatory Tests and Timing) [MPH]

Purpose:
To ensure the **safety of RNA therapeutics**.
Content:
Vital signs & neurological assessment: ICE score
Blood tests: CBC, biochemistry, CRP, ferritin, IL-6
Cardiotoxicity monitoring: Troponin, BNP, ECG
Complement-related markers: C3a, C5a, anti-PEG IgM/IgG
Schedule:
0 h, 6–12 h, 24 h, 72 h, Day 7, Day 14, Day 28
Notes / Actions:
Follow the **dosing and blood sampling timeline**

M: Rodent – Mouse (Preclinical studies)
R: Rodent – Rat (Preclinical studies)
C: Canine – Dog (Preclinical studies)
P: Primate (Preclinical studies)
H: Human – First-in-Human (FIH) trial

③ LNP-related Adverse Event Risks and Management [PH]

Purpose:
To address concerns related to RNA/polymer administration.
Content:
Acute: CARPA, anaphylaxis → Stepwise dosing + rescue medications
Subacute: Hepatotoxicity → Regular AST/ALT monitoring
Immunologic: Anti-LNP antibodies, ABC phenomenon → Short-term, self-limited protocol + antibody measurements
Chronic: No cumulative toxicity (ensured by transient RNA expression)
Notes / Actions:
The summary of adverse event risks vs management strategies is as follows

Table: LNP/RNA Adverse Event Risks and Management

Risk Category	Specific Risk	Onset Timing	Management (Prophylaxis / Monitoring / Rescue)
Acute Immune Reactions	CARPA (complement activation–related pseudoallergy), Anaphylaxis	Immediately to several hours post-infusion	- Stepwise dosing (10–20% → remainder) - Observation 30–40 min post-infusion - Rescue meds: epinephrine, antihistamines, corticosteroids
Acute Immune Reactions	CARPA (complement activation–related pseudoallergy), Anaphylaxis	Immediately to several hours post-infusion	- Stepwise dosing (10–20% → remainder) - Observation 30–40 min post-infusion - Rescue meds: epinephrine, antihistamines, corticosteroids
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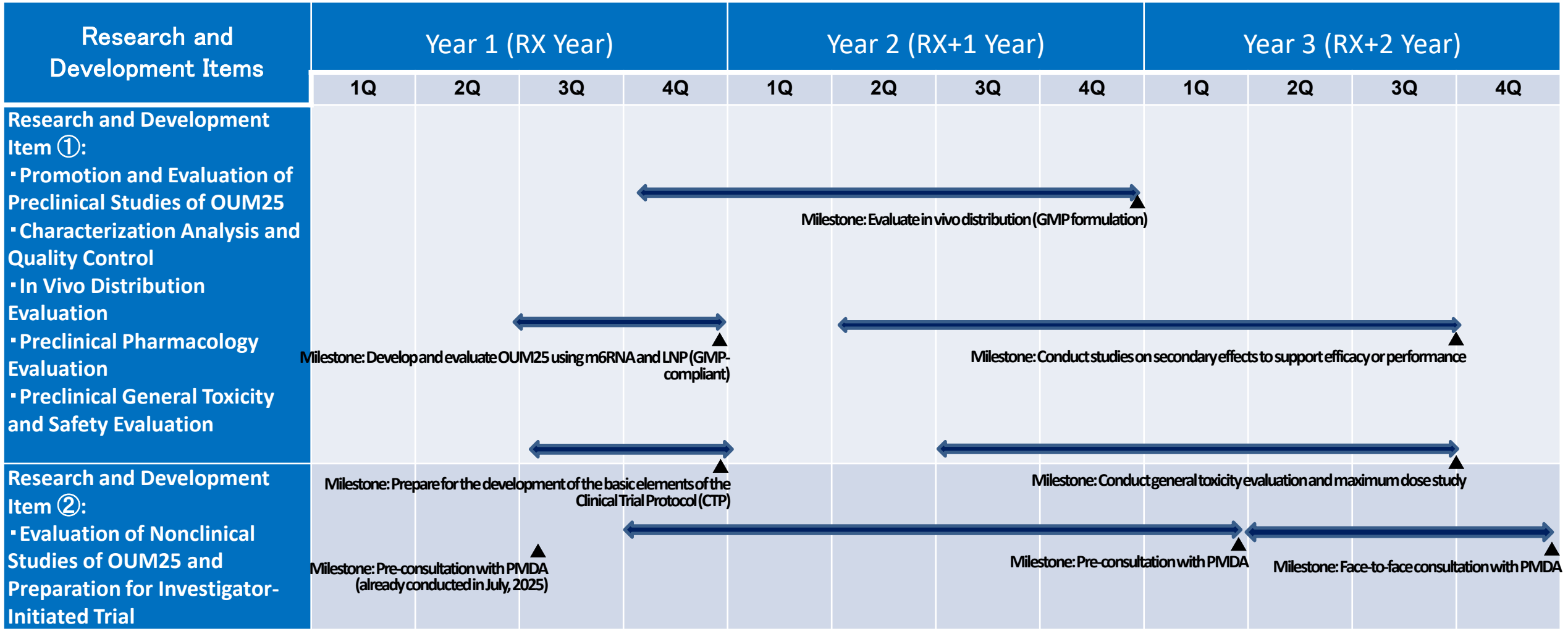
④ Liver Function Monitoring (Hepatotoxicity Monitoring)[MRCPH]

Purpose:
To address concerns related to **LNP administration**.
Content:
Hepatic enzymes: AST, ALT, LD, ALP
Imaging studies: CT, ultrasound (US)
Immunologic monitoring: Anti-PEG antibodies, ABC phenomenon
Antigen testing: LNP, RNA sequencing
Management / Actions:
Follow guidelines similar to **gastrointestinal disease monitoring**
Intensive monitoring for early detection of hepatotoxicity or immune-related events

Table: Liver Imaging – Animal Models vs Humans

Modality	Small Animals (Mouse / Rat)	Large Animals (Dog / Non-human Primates)	Humans
CT	- Resolution / slice thickness: 50–200 µm (micro-CT); clinical small-animal CT: 0.5–1.0 mm - Scan time: 5–20 min (under general anesthesia) - Cost: 30,000–50,000 JPY per scan (facility-dependent) - Applications: Tumor volume assessment, fatty liver models, fibrosis, drug-induced liver structural changes	- Resolution / slice thickness: 0.5–1.0 mm (comparable to clinical CT) - Scan time: 5–10 min (under sedation) - Cost: 50,000–100,000 JPY per scan (species/institution dependent) - Applications: Biliary obstruction, liver tumors, chronic hepatitis, drug toxicity evaluation	- Resolution / slice thickness: 0.5–1.0 mm (≥64-slice multislice CT) - Scan time: tens of seconds (breath-hold) - Cost: 20,000–50,000 JPY (insurance-covered) - Applications: Hepatitis, cirrhosis, liver tumors, acute liver failure morphology, portal vein flow evaluation (with contrast)
US	- Resolution / slice thickness: 30–100 µm (high-frequency probe 20–40 MHz) - Scan time: 5–15 min (light anesthesia) - Cost: 10,000–30,000 JPY per scan - Applications: Tumor size evaluation, fatty liver, fibrosis scoring (elastography)	- Resolution / slice thickness: 0.2–0.5 mm (clinical equipment) - Scan time: 5–10 min - Cost: 30,000–50,000 JPY per scan - Applications: Cirrhosis, fatty liver, hemodynamics, tumor size and number evaluation	- Resolution / slice thickness: ~0.5–1.0 mm (clinical probe 2–10 MHz) - Scan time: few minutes to 10 min - Cost: 10,000–20,000 JPY (insurance-covered) - Applications: Chronic hepatitis, cirrhosis, fatty liver, acute liver failure progression, portal hypertension assessment

Preclinical Animal Study Research Plan (Short-term and Mid-term Plans)



Preclinical Study Schedule (Adverse Events (CRS, ICANS):

Adverse events will be evaluated on predetermined assessment days using predefined parameters (blood tests and imaging).
CRS management: Focus on ultrasound and serum marker assessments.
LNP-related adverse events: Emphasis on CARPA, myocarditis, and hepatotoxicity.

Examination of dosage and administration of m6A_CART/DDS

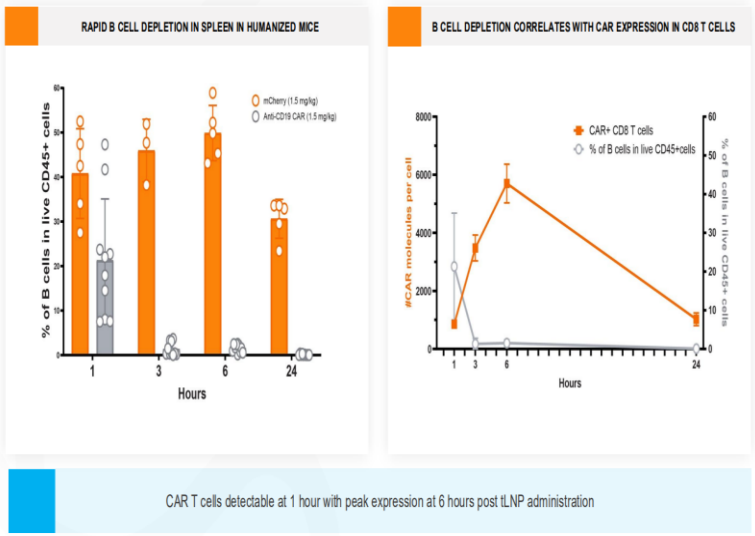
Reference materials

DATA that serve as the basis for considering the "administration interval" based on pharmacokinetics

[2024-acr-presentation_patient-sample-vf.pdf]

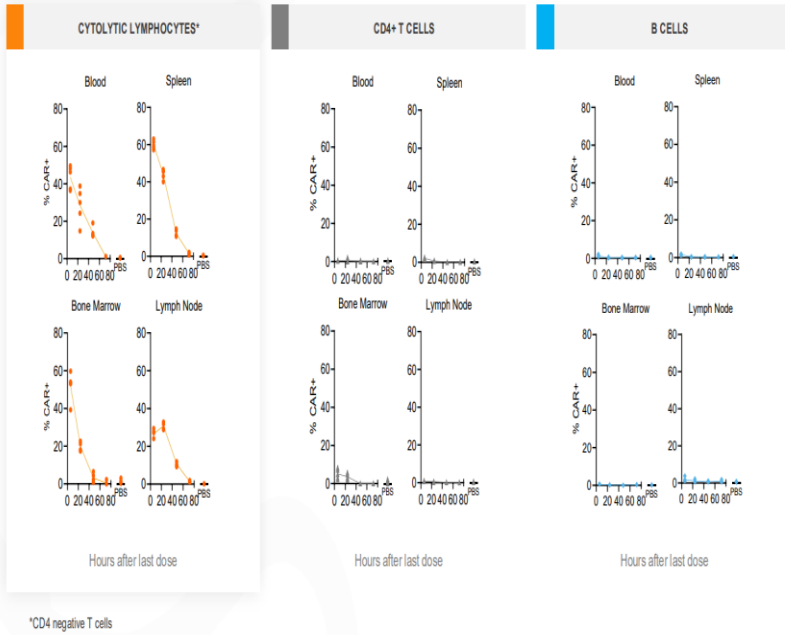
Effective Engineering of CD8+ T Cells from Autoimmune Disease Patients Utilizing a CD8-Targeted Lipid Nanoparticle Encapsulating an Anti-CD19 CAR mRNA (CPTX2309)
C a p s t a n T h e r a p e u t i c s

CPTX2309 Administration to Humanized Mice Results in Rapid and Complete Depletion of Engrafted Human B Cells



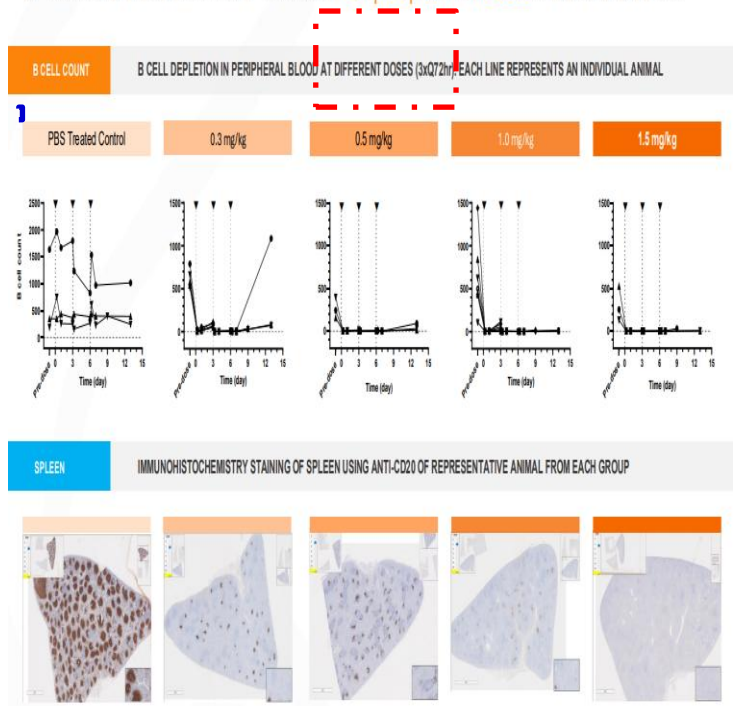
In m6A_CART, the trough value was set at 48 hours, taking into account a safety margin.

Rapid and Preferential In Vivo Engineering of CAR-T Cells in Blood and Tissue
Biodistribution Study in Mouse with CPTX2309



m6A_CART is expected to efficiently reach immune cells (spleen, lymphatic tissue, TLS, etc.).

CPTX2309-S Treatment in NHP Results in Deep Depletion of B cells in Blood and Tissue



- For m6RNA_CART, the therapeutic dose is estimated to be 0.5-1 mg/kg RNA equivalent.
- The MABEL (Minimum Biologically Effective Level) is 0.3 mg/kg RNA equivalent or less.
- The MTD (Maximum Tolerated Dose) will be determined in this study.

Summary of dosage setting (provisional, reference)

Reference materials

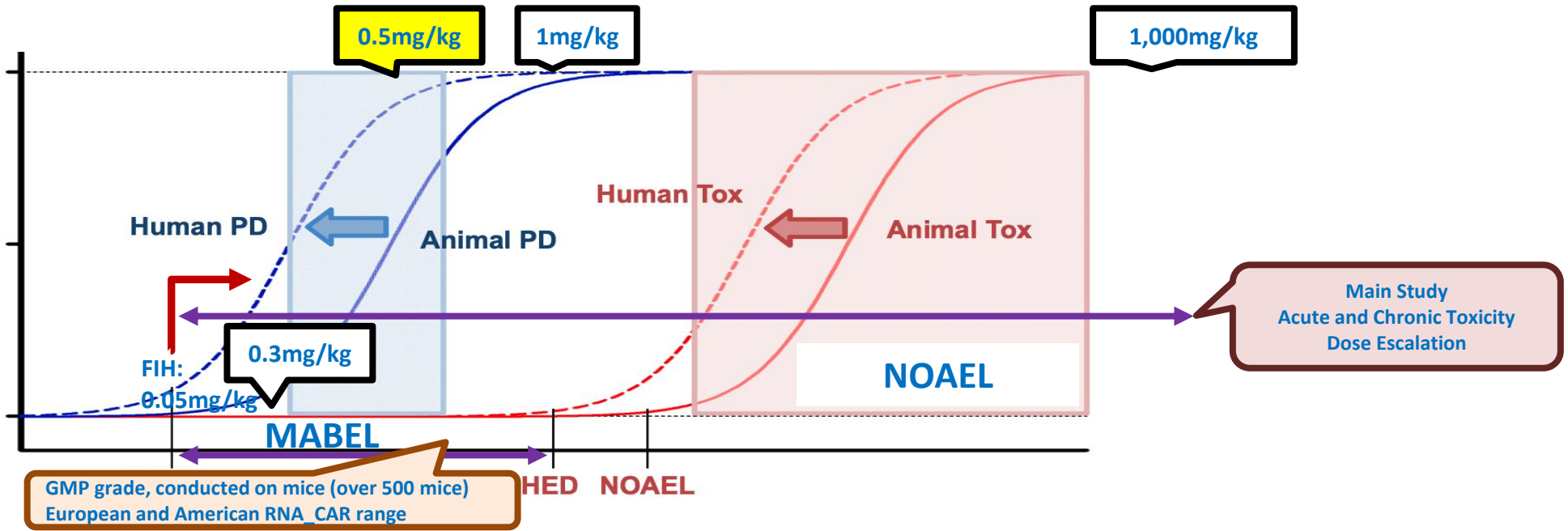
The determination of the first-in-human dose.

NOAEL (No Observed Adverse Effect Level) Approach.

Determine the no-toxic dose in animals through non-clinical trials, and then determine the initial dose taking into account the safety factor.

MABEL (Minimum Anticipated Biological Effect Level) Approach.

The dose that exerts the minimum pharmacological effect is estimated from non-clinical trials (in vivo, in vitro) that reflect the mechanism of action of the drug, and the initial dose is set taking into account a safety factor as necessary.



M: Rodent – Mouse (Preclinical studies)
R: Rodent – Rat (Preclinical studies)
C: Canine – Dog (Preclinical studies)
P: Primate (Preclinical studies)
H: Human – First-in-Human (FIH) trial
HED : Human Equivalent Dose

Timeline: Collaboration → Global Expansion

PoC in Animal Models → FIH Study

From proving the science to building a global RNA healthcare industry—early participation puts you at the forefront of the RNA therapeutics × CAR-T × diagnostics market.

Phase	Project Duration	Technical & Business Milestones	Participation Opportunities for Interested Stakeholders	Expected financial returns and potential exit opportunities
Phase 1：PoC Establishment *"Science becomes Proof"*	-2025～2028	・Fibrotic region detection algorithm via RNA modification ・Early in vivo efficacy of target-specific RNA-modified CAR-T ・University hospital PoC initiation	・Commercialization promoters & Japanese public funding (AMED/JST) ・Seed investment & joint PoC support (university VCs / healthcare CVCs)	Although technical risks are high, this is the phase for securing exclusive patents and proprietary knowledge.
Phase 2：Development and Commercialization Strategy *"Proof becomes Business"*	2029～2030	・OEM Launch of Liquid Biopsy Diagnostic Kits ・Joint Development Agreements & Milestone Achievements with Pharma ・PCT Filings Completed & Freedom-to-Operate (FTO) Secured	Pharma strategic investment & VC funding with collaborative research	At this stage, the project achieves initial domestic profitability and licensing value becomes tangible, making investment recovery feasible.
Phase 3：Expansion into Global Markets *"Business becomes Global"*	2031～2033	・Global collaborative clinical PoC (Europe, US, Asia) – industry partnerships ・GMP production of novel DDS & international standardization ・RNA therapeutics data platform establishment	Strategic expansion targeting international markets	Forming strategic alliances with leading international pharmaceutical companies, targeting a corporate valuation of approximately 10 billion yen.
Phase 4：Global RNA Medicine Company へ *"Japan-origin, World-standard"*	2034～	・Integrated RNA medicine business: diagnostics, therapeutics & drug discovery support ・International regulatory compliance (FDA / EMA / PMDA)	Reinvesting and expanding collaborative development activities	The project aims for a public listing or acquisition exit as a global, next-generation DDS RNA therapeutics business.

Reference（Patents / Key Papers）

Patents

Our seed technology holds a unique competitive advantage through: (i) filed foundational patents, (ii) a triple-layer defense comprising m⁶A modification, FAP-targeting sequences, and LNP formulation, and (iii) secured First-in-Human (FIH) positioning.

Platform 1 – RNA (Active Pharmaceutical Ingredient Patents)
- Japanese patent application: JP 2024-058159, filed on March 29, 2024
- PCT application: PCT/JP2025/012812, filed on March 28, 2025
- Title of invention: Cell Therapy
- Inventors: Hideshi Ishii et al. (6 others)
- Applicant: The University of Osaka

Platform 2 – DDS (RNA Drug Carrier Patents)
- Japanese patent application: JP 2021-1131189, filed on July 7, 2021
- PCT application: PCT/JP2022/026863, filed on July 6, 2022
- Title of invention: Lipid Derivatives
- Inventors: Hiroshi Miura (collaborator) et al. (9 others)
- Applicants: Tokyo University of Science, Nisshin Oil Mills Co., Ltd.

Platform 3 – Material/Application (RNA Drug + Carrier Patents)
- Inventors: Hideshi Ishii, Hiroshi Miura
- Applicants: The University of Osaka, Tokyo University of Science
- Filed: September 2025

Platform 4 – Companion Diagnostic Technology (MS + TS Patents)
- **MS**: JP 2018-30099; PCT/JP2019/6588; WO2019/163900
- **TS**: JP 2019-85805; PCT/JP2020/017654

Key Papers

Targeting fibroblast activation protein in solid tumors via LNP-mediated CAR-mRNA delivery promotes durable regression in murine models.
Meng S, Hara T, Sato T, Tatekawa S, Arao Y, Saito Y, Hirai T, Motooka D, Rennie S, Satoh T, Ogawa K, Miura Y, Mori M, Doki Y, Eguchi H, Ishii H.Sci Rep. 2025 Dec 10. doi: 10.1038/s41598-025-31128-5. Online ahead of print.PMID: 41366016

In Vivo Engineered CAR-T Cell Therapy: Lessons Built from COVID-19 mRNA Vaccines.
Meng S, Hara T, Miura Y, Arao Y, Saito Y, Inoue K, Hirotsu T, Vecchione A, Satoh T, Ishii H.Int J Mol Sci. 2025 Mar 28;26(7):3119. doi: 10.3390/ijms26073119.PMID: 40243757

Fibroblast activation protein constitutes a novel target of chimeric antigen receptor T-cell therapy in solid tumors.
Meng S, Hara T, Miura Y, Ishii H.Cancer Sci. 2024 Nov;115(11):3532-3542. doi: 10.1111/cas.16285. Epub 2024 Aug 21.PMID: 39169645

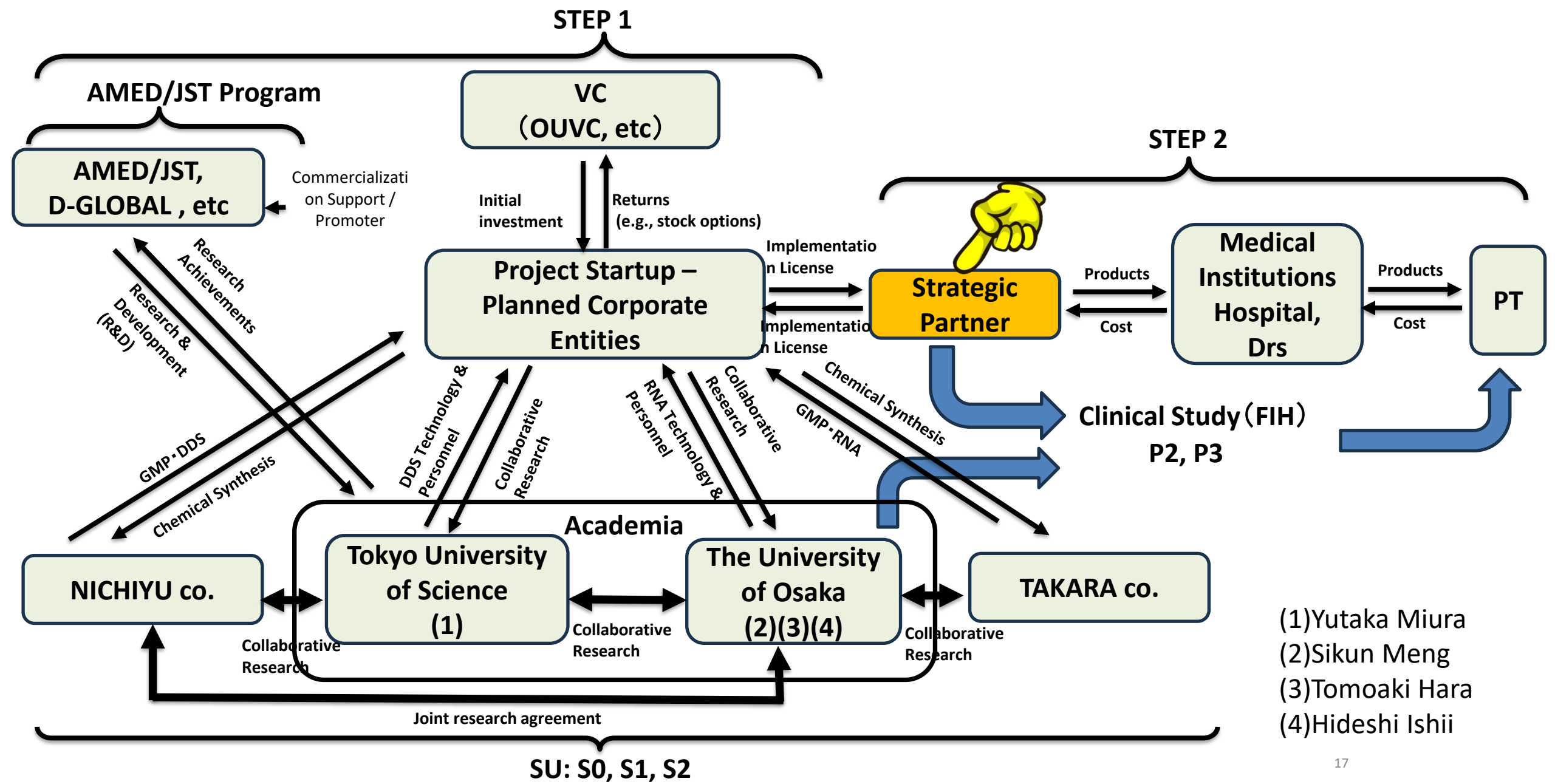
Tissue-Resident Memory T Cells in Gastrointestinal Cancers: Prognostic Significance and Therapeutic Implications.
Sato H, Meng S, Hara T, Tsuji Y, Arao Y, Sasaki K, Kobayashi S, di Luccio E, Hirotsu T, Satoh T, Doki Y, Eguchi H, Ishii H.Biomedicines. 2024 Jun 17;12(6):1342. doi: 10.3390/biomedicines12061342.PMID: 38927549

RN7SL1 may be translated under oncogenic conditions.
Hara T, Meng S, Tsuji Y, Arao Y, Saito Y, Sato H, Motooka D, Uchida S, Ishii H.Proc Natl Acad Sci U S A. 2024 Mar 19;121(12):e2312322121. doi: 10.1073/pnas.2312322121. Epub 2024 Mar 13.PMID: 38478683

High N6-methyladenosine-activated TCEAL8 mRNA is a novel pancreatic cancer marker.
Hara T, Meng S, Sato H, Tatekawa S, Sasaki K, Takeda Y, Tsuji Y, Arao Y, Ofusa K, Kitagawa T, Yamada D, Takahashi H, Kobayashi S, Motooka D, Suzuki Y, Rennie S, Uchida S, Mori M, Ogawa K, Doki Y, Eguchi H, Ishii H.Cancer Sci. 2024 Jul;115(7):2360-2370. doi: 10.1111/cas.16152. Epub 2024 Apr 24.PMID: 38659235

pH-responsive polyzwitterion covered nanocarriers for DNA delivery.
Shen X, Dirisala A, Toyoda M, Xiao Y, Guo H, Honda Y, Nomoto T, Takemoto H, Miura Y, Nishiyama N.J Control Release. 2023 Aug;360:928-939. doi: 10.1016/j.jconrel.2023.07.038. Epub 2023 Jul 28.PMID: 37495117

Team Members & Research Structure



(1)Yutaka Miura
(2)Sikun Meng
(3)Tomoaki Hara
(4)Hideshi Ishii

Proposed Partnership Scheme

Strategic Collaboration Proposal

We are advancing the development of **FAP_CART**, an RNA therapeutic enabled by our novel **polybetain-based drug delivery system (DDS)**. A strategic partnership with a global pharmaceutical company would create strong synergies, providing clear value and risk-reduction across the development pipeline.

1. Accelerated Development and Market Entry of FAP_CART
Key Advantages for Industry Partners
Rapid initiation of FIH trials in Japan through support for GMP-grade manufacturing, nonclinical safety studies (rodent and non-rodent), and pharmacology studies.
Reduced development risk by leveraging regulatory expertise tailored to PMDA, FDA, and EMA pathways.
Early strategic positioning for global commercialization by engaging from the first-in-human stage and shaping clinical and regulatory strategies from the outset.
Risk-Mitigation Factors
Backing from **AMED** and the **Osaka University Center for Future Medical Care** significantly reduces early-stage financial and operational burden.
Robust nonclinical study designs based on extensive prior data minimize safety uncertainties at clinical transition.

2. Expansion of the Polybetain DDS as a Multi-Disease Platform
Platform Advantages
Demonstrated efficacy not only for FAP, but also for **HER2** and **cancer stem cell markers**, enabling broad therapeutic applicability.
Strong potential for expansion into indications with clear antigenic targets, including **endometrial disorders, neurodegenerative diseases, and retinal diseases**—opening new market opportunities.
Opportunity to **co-develop and secure IP** for a next-generation RNA delivery platform, ensuring long-term competitive advantage.
Risk-Mitigation Factors
A platform-based approach diversifies therapeutic targets, reducing dependency on a single indication.
Early accumulation of scientific and safety data lowers regulatory uncertainty for subsequent assets built on the same DDS backbone.

3. Strategic Market Advantages
Pursuit of **early regulatory approvals** in Japan and global markets positions the partner as a first mover in a rapidly expanding RNA therapeutics landscape.
A disease-agnostic platform enables flexible future **pipeline expansion** and **licensing strategies**, strengthening long-term portfolio resilience.
Early-stage collaboration allows joint optimization of **formulation development, manufacturing scale-up, and global supply strategy**.

Conclusion
This collaboration offers **a low-risk, high-upside opportunity** to co-create a transformative RNA therapeutic and a scalable DDS platform. Together, we can accelerate clinical translation, secure global regulatory success, and lead the next wave of precision RNA medicine.

Executive Summary

Harnessing a next-generation polymer platform for RNA therapeutics, we target immune-driven fibrosis in gastrointestinal organs at its inception, unlocking treatment for previously intractable diseases.