National Cancer Center (NCC) Japan, NCC Seed Acceleration Program（NCC SAP）

# Development of versatile TCR-T cell therapy targeting inducible public splice-neoantigens

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## Vision

- We aim to overcome the major challenges in TCR-T cell development for cancer—limited patient eligibility and high individualized development costs—by making TCR-T therapy more broadly applicable.
- Although TCR-T cells can show remarkable efficacy, target antigen expression in solid tumors is often limited, restricting eligible patients and response rates. Individualized manufacturing and adverse-effect management also remain key barriers.
- RECTAS3.0 induces public cancer antigens (iPSNA). TCR-T targeting iPSNA enables a broader patient population, improving manufacturing efficiency, accelerating clinical development, and enabling reversible control of potential adverse effects.

## Marketability

- Tecelra is currently the only FDA-approved TCR-T therapy, targeting MAGE-A4 in HLA-A*02-positive synovial sarcoma. Demonstrating broad efficacy of this program across solid tumors could transform cancer immunotherapy.
- For ICI-nonresponsive colorectal cancer in Western countries, assuming 300,000 cases/year, 30% HLA-A*02:01 positivity, and 1% initial penetration, the addressable market could reach several hundred million USD annually.
- To our knowledge, there are no direct competitors targeting pharmacologically induced cancer antigens with TCR-T cells.

## Innovation

This program is innovative in that it enables cancer-agnostic treatment using universal TCR-T cells targeting iPSNA. Although a U.S. group has reported a splicing neoantigen induction strategy using indisulam, immunotoxicity has been reported with this approach. In contrast, RECTAS3.0, the compound used in this program, has demonstrated an extremely favorable safety profile in preclinical studies, providing a clear competitive advantage.

## Partnering

**【 Expected partners 】**
Pharmaceuticals・Biotech/Drug Discovery Service・CMO/CDMO/CRO/SMO・Venture capitals
**【 Expectation 】**
Identification of potential CDMO partners for TCR-T cell manufacturing, establishment of a TCR-T cell manufacturing pipeline, evaluation of required testing items for future clinical trials, and startup support.

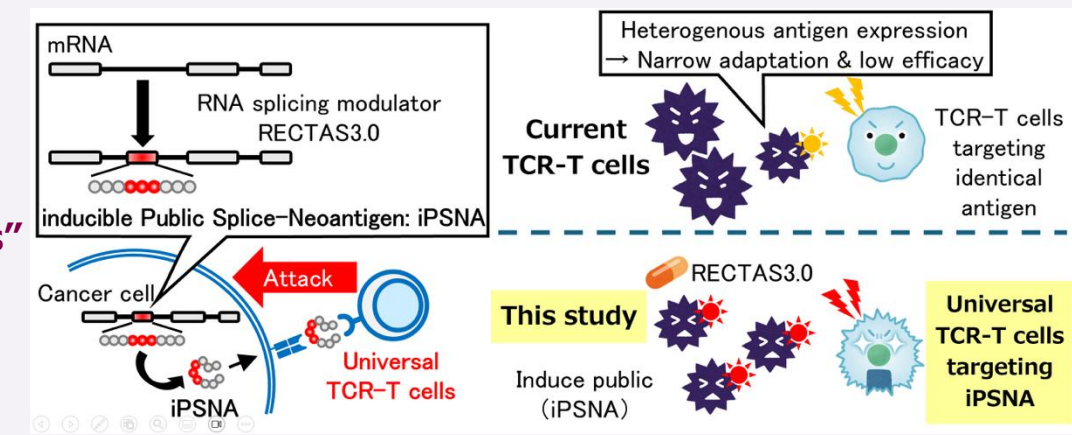
## Research Outline

Key Words: #TCR-T, #Public antigen, #RNA splicing, #Small compound

【Seed Technology】

- The splicing modulator RECTAS3.0 induces the expression of iPSNA, a cancer antigen commonly shared across various cancer types.
- TCR-T cells targeting the shared antigen iPSNA are generated.
- After inducing iPSNA expression in cancer cells with RECTAS3.0, iPSNA-targeted TCR-T cells will be administered.

➡ **This approach enables the development of "universal TCR-T cells" that are effective against a much broader range of cancer types than conventional TCR-T cells.**




【Objective of This Study】

- To demonstrate that universal TCR-T cells have sufficient antitumor efficacy to support clinical trials and eventual product development.

【Goal of this study】

- To advance toward early clinical studies, we will select the optimal iPSNA peptide sequence, iPSNA-specific TCR sequence, and target cancer type.
- To obtain in vivo proof of concept by demonstrating the antitumor efficacy of universal TCR-T cells in human tumor-bearing mouse models.

【References】Matsushima, et al. (2022) Sci Transl Med 14:eabn6056.

【Intellectual Property Imformation】① PCT/JP2023/039985: Quinazoline derivatives, ② PCT/JP2023/039979: Nitrogen-containing heterocyclic compound, ③ PCT/JP2022/033464: Improvement of tumor immunogenicity by means of splicing-controlling compound.

Summary: Splicing modulators, Treatment of aberrant splicing-derived diseases, improvement of tumor immunogenicity