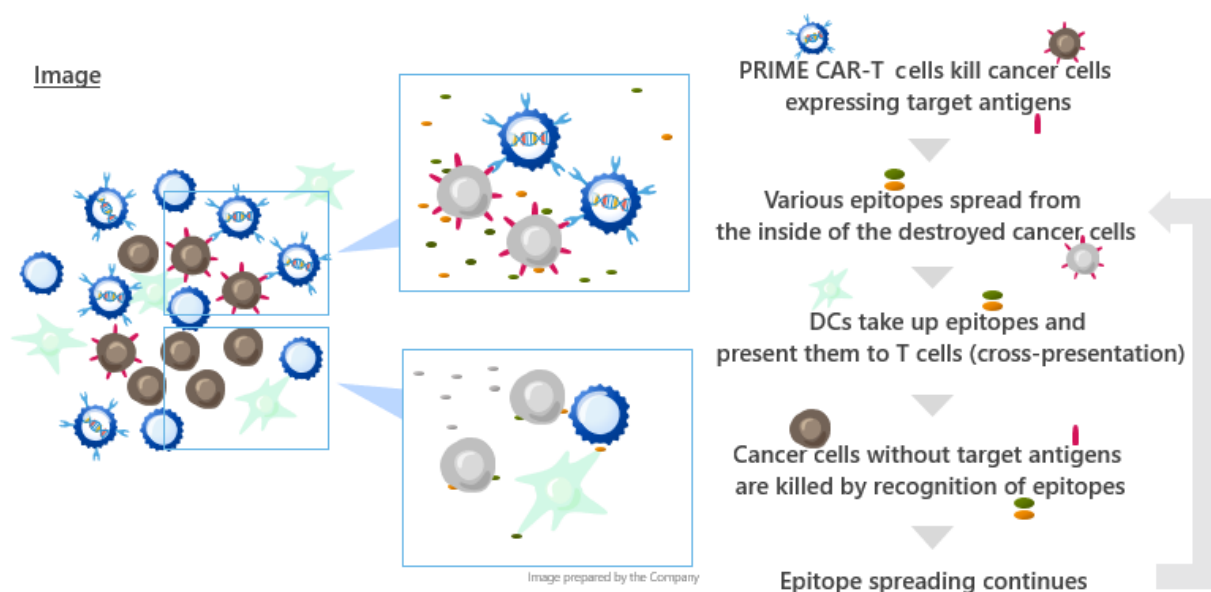


**Poster Presentation at the Society for Immunotherapy of Cancer (SITC)  
Mechanism of Action for the Anti-Tumor Effects of CAR-T Cells Expressing IL-7 and CCL19:  
Suggesting the Potential Therapeutic Efficacy of PRIME CAR-T Cells**

Noile-Immune Biotech, Inc. (2-12-10 Shiba-Daimon, Minato-ku, Tokyo, President & CEO: Koji Tamada, hereinafter "Noile-Immune"), in joint research with Yamaguchi University Graduate School of Medicine (hereafter referred to as Yamaguchi University), has presented a poster at the 38th Annual Meeting of the Society for Immunotherapy of Cancers (SITC), held in San Diego from November 1st to November 5th, 2023, on the study results using a mouse solid cancer model concerning the mechanism of action for the anti-tumor effects of CAR-T cells expressing Interleukin-7 (IL-7) and CCL19 (referred to as 7×19 CAR-T cells).

The study results indicated that the robust anti-tumor effects exhibited by 7×19 CAR-T cells involve the induction of epitope spreading<sup>\*\*2</sup> to endogenous tumor antigens, associated with an increase in dendritic cells capable of cross-presentation<sup>\*\*1</sup>. This suggests that the destruction of cancer cells possessing the CAR target by 7×19 CAR-T cells leads to the release of new antigens distinct from the CAR target, the uptake of which by dendritic cells presents new antigen epitopes, thereby activating the host's T cells and exhibiting anti-tumor effects. This indicates the potential of 7×19 CAR-T cells to exert therapeutic effects on solid cancers with antigen heterogeneity or cancer tissues where mutated cells have emerged with loss of the CAR target.

Noile-Immune is advancing the development of 7×19 CAR-T cells, which are termed "PRIME CAR-T cells (Proliferation-inducing and migration-enhancing CAR-T cells)" due to their characteristics. For more details, please visit [https://www.noile-immune.com/en/Our\\_Science/prime\\_car-t.html](https://www.noile-immune.com/en/Our_Science/prime_car-t.html).



\*1: Some dendritic cells have the ability to ingest extracellular antigens, process them, and present the epitopes to T cells on MHC class I molecules. This phenomenon is referred to as cross-presentation.

\*2: An epitope is the part of an antigen that is recognized by antibodies or T cell receptors. Epitope spreading refers to the process during the immune response where the reaction to the initially targeted epitope causes new epitopes to be presented to immune cells, leading to a continuous immune response to these new epitopes.

### **Background:**

CAR-T cell therapy against hematological malignancies demonstrated potent therapeutic efficacy, resulting in clinical application of these treatments. On the other hand, CAR-T cell therapy against solid cancers has yet to be fully developed, as only a few exceptional cases have been reported to demonstrate clinical efficacy. Potential hurdles for the effects of CAR-T cell therapy in solid cancers include heterogeneity of tumor-associated targets, insufficient migration and infiltration of CAR-T and endogenous immune cells into tumor tissues, and immunosuppressive nature of tumor microenvironment.

### **Summary of Presentation:**

The collaborative research team from Noile-Immune and Yamaguchi University conducted an immunological mechanism study to investigate the anti-tumor effects of 7×19 CAR-T cells using a mouse solid cancer model. The key observations from the study include:

- The administration of 7x19 CAR-T cells resulted in the complete regression of solid tumors in a mouse model.
- The administration of 7x19 CAR-T cells led to the infiltration of T cells and dendritic cells in the tumor tissue of mice.
- The removal of the host T cells resulted in the attenuation of the anti-tumor effect of 7×19 CAR-T cells.
- The administration of 7x19 CAR-T cells induced T cells responsive to endogenous tumor antigens in tumor-bearing mice, confirming epitope spreading.
- The administration of 7x19 CAR-T cells induced an increase in dendritic cells with cross-presentation capability.
- The therapeutic effects of 7x19 CAR-T cells were observed even in the mixture of CAR target-positive and negative tumor cells.

### **Detailed Information:**

- Presenter: Keishi Adachi<sup>1</sup>, Yukimi Sakoda<sup>1,2</sup>, Koji Tamada<sup>1,2</sup>
- Affiliations: 1. Yamaguchi University Graduate School of Medicine; 2. Noile-Immune Biotech Inc.
- Reference: Adachi K, Kano Y, Nagai T, Okuyama N, Sakoda Y, Tamada K. IL-7 and CCL19 expression in CAR-T cells improves immune cell infiltration and CAR-T cell survival in the tumor. *Nat Biotechnol.* 2018 Apr;36(4):346-351. doi: 10.1038/nbt.4086. Epub 2018 Mar 5.

### **Notes on the Press Release:**

- The information is derived from a conference presentation and may change during publication.
- This press release contains forward-looking statements.

**Noile-Immune Biotech Inc., established as a university start-up, aims to contribute to the arrival of an era when we can overcome cancer through the next-generation cancer immunotherapies, centering on PRIME technology.**

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