

# PROTEIN USED TO ENHANCE T CELL EXPANSION TO IMPROVE CANCER IMMUNOTHERAPY

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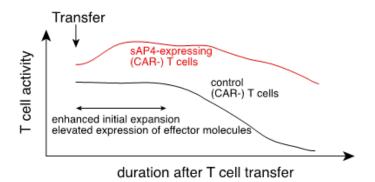
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**Value Proposition:** This invention utilizes a protein to enhance T cell expansion for CAR-T cell therapy and other adoptive cellular immunotherapy.

## **Technology Description**

Researchers at Washinton University in St. Louis have developed a mutant AP4 protein that is designed to reduce the time and expense of *ex vivo* T cell expansion for adoptive cellular immunotherapy, including CAR-T cell cancer immunotherapy. AP4 is a transcription factor that amplifies and prolongs CD8+ T cell-mediated immune response following induction and maintenance by the cytokine Interleukin-2 and the transcription factor c-Myc. Therefore, this protein could potentially counteract T cell exhaustion in cancer immunotherapy. However, wild type AP4 is an unstable protein with a short half-life (2-3 hours) and requires constitutive Interleukin-2 receptor signals.

This technology increases the half-life of AP4 to 48 hours by introducing at single mutation that enhances stability without affecting function, thus making its expression independent of the natural activator Interleukin-2. By maintaining the cellular programs of T cells, mutant AP4 could maximize T cell expansion and effector differentiation to improve immunotherapy.



#### **Stage of Research**

The inventors have confirmed that the mutant AP4 is functional and that it resists degradation when expressed ectopically in CD8+ T cells. They have also demonstrated that the half-life of mutant AP4 is ~48 hours (compared to wild type AP4 which has a half-life of 2-3 hours).

#### **Publications**

• **Chou** C, Verbaro DJ, Tonc E, Holmgren M, Cella M, Colonna M, Bhattacharya D, **Egawa** T. (2016). <u>The Transcription Factor AP4 Mediates Resolution of Chronic Viral Infection through Amplification of Germinal Center B Cell Responses.</u>



Immunity. 2016 Sep 20;45(3):570-582. doi: 10.1016/j.immuni.2016.07.023. Epub 2016 Aug 23. PMID: 27566940

• Chou C, Pinto AK, Curtis JD, Persaud SP, Cella M, Lin CC, Edelson BT, Allen PM, Colonna M, Pearce EL, Diamond MS, Egawa T. (2014). c-Myc-induced transcription factor AP4 is required for host protection mediated by CD8+ T cells. Nat Immunol. 2014 Sep;15(9):884-93. doi: 10.1038/ni.2943. Epub 2014 Jul 13. PMID: 25029552

### **Applications**

Cancer immunotherapy

## **Key Advantages**

- Prolonged T cell proliferation, activation and differentiation
- Reduces the time and expense of ex vivo T cell expansion
- Compatible and synergistic with autologous T cell therapy and checkpoint inhibitors

#### **Patents**

• Ap4 and methods of promoting t cell activation (PCT Application, Publication No. WO2018075941A1)

Related Web Links - Takeshi Egawa Profile; Egawa Lab