

# PROTEIN TO ENHANCE T CELL EXPANSION FOR CAR-T CELL THERAPY AND OTHER ADOPTIVE CELLULAR IMMUNOTHERAPY

[Chou, Chun, Egawa, Takeshi](#)

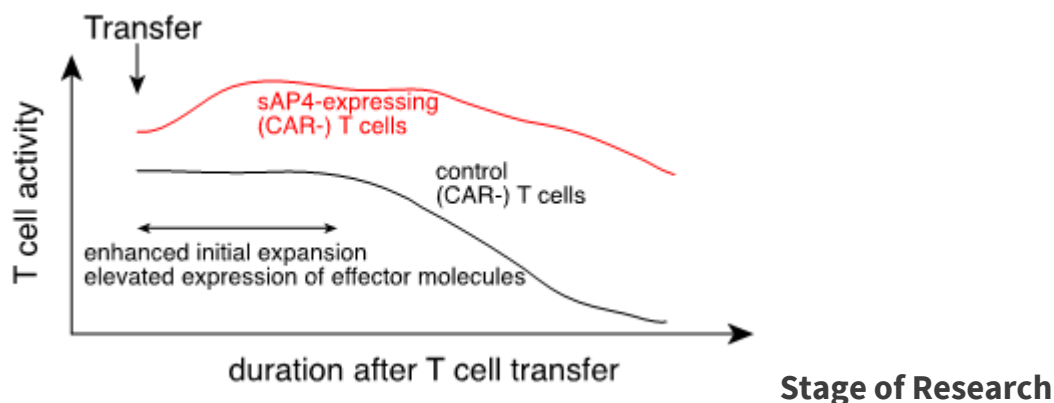
[Han, Nathan](#)

T-016284

## Technology Description

Researchers in Prof. Takeshi Egawa's laboratory 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 IL-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 IL-2 receptor signals.

This technology increases the half-life of AP4 to 48 hours by introducing a single mutation that enhances stability without affecting function, thus making its expression independent of the natural activator IL-2. The resulting mutant AP4 could be introduced to cytotoxic T cells *ex vivo* to boost their activity and functionality. These effects are compatible and synergistic with both autologous T cell therapy and checkpoint inhibitors. By maintaining the cellular programs of T cells, mutant AP4 could maximize T cell expansion and effector differentiation to improve immunotherapy.



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).

## Applications

- **Cancer immunotherapy** – improve CD8+ T cell proliferation for downstream use in CAR-T cell therapy and other adoptive cellular immunotherapy therapies

## Key Advantages

- **Prolonged T cell proliferation, activation and differentiation** independent of the natural activators IL-2 and c-Myc
- **Reduced cost and time:**
  - with enhanced proliferation, the cost and time of in vitro expansion could potentially be reduced by generating therapeutic effects with a smaller number of cells
  - no tumor antigen screen needed because AP4 enhancement is independent of tumor specific antigen
- **Synergistic effects** – compatible and synergistic with autologous T cell therapy and checkpoint inhibitors

## Publications

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

## Patents

- [Ap4 and methods of promoting t cell activation](#) (PCT Application, Publication No. WO2018075941A1)