Washington University in St. Louis
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PROTEIN USED TO ENHANCE T CELL EXPANSION TO IMPROVE CANCER IMMUNOTHERAPY

Chou, Chun, Egawa, Takeshi

Han, Nathan

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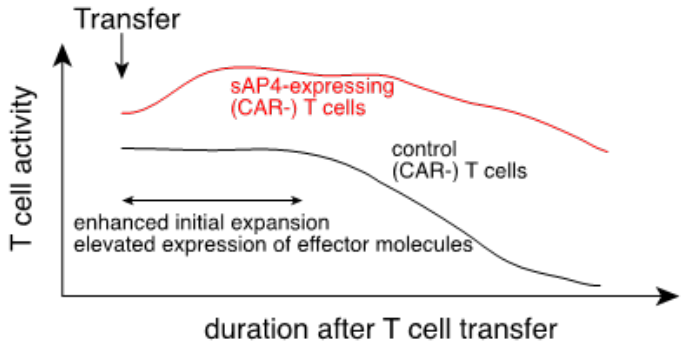
Value Proposition: *This invention utilizes a protein to enhance T cell expansion for CAR-T cell therapy and other adoptive cellular immunotherapy.*

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). 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

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