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One-step mixing with anti-tumor/anti-CD3 bispecific antibody enhances tumor targeting and therapeutic efficacy of *ex vivo* expanded T cells

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Adoptive T cell transfer, involving the *ex vivo* expansion of cancer patient's T cells and then intravenous injection back to the patient, can effectively mediate tumor regression and extend patient's life. However, lack of tumor specificity of most expanded T cells and time-consuming of generating tumor-specific T cells severely restrict *in vivo* survival time and anti-cancer ability of these *ex vivo* expanded T cells. In this study, we developed bispecific antibodies (BsAbs) by fusing an anti-CD3 scFv to the C-terminus of a Fab against tumor-associated antigen, such as EGFR or PSMA, to form α-tumor/α-CD3 BsAbs. The anti-CD3 end of the BsAb could non-covalently bind to CD3+ T cells and the anti-tumor end of BsAb can endow T cells with specificity to EGFR+ or PSMA+ tumor cells. One-step mixing with BsAbs significantly enhanced the killing efficacy of CD3+ T cells against EGFR+ colon cancer cells and PSMA+ prostate cancer cells in vitro and *in vivo*. Contact of BsAb-armed T cells with EGFR+ or PSMA+ tumor cells dramatically increase the release of cytotoxic factors, including: perforin, granzyme, INF-γ, and TNF-α, from these T cells to kill tumor cells. The α-tumor/α-CD3 BsAbs offer a simple one-step method to confer tumor specificity to CD3+ T cells for enhanced tumor targeting and improved therapeutic efficacy.

Biography

Kuo-Hsiang Chuang completed his PhD degree in Biomedicine at Kaohsiung Medical University, Taiwan, in 2010. From March 2010 to January 2012, he joined Professor Tian-Lu Cheng's group (Kaohsiung Medical University) as a Post-doctoral Fellow to study protein engineering, including the development of humanized antibodies and novel recombinant protein drugs. In February 2012, he became an Assistant Professor in Graduate Institute of Pharmacognosy, Taipei Medical University, Taiwan. Now, he focuses on several research fields, including: Reporter genes/non-invasive imaging systems, antibody engineering, immunotherapy, and type 1 diabetes.

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